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Clinical Section

President—BERNARD MYERS, C.M.G., M.D.

[*Febuary* 9, 1934.]

Calcinosis Universalis.—J. H. SHELDON, M.D. (Wolverhampton).

R. B., male aged 20. Quite healthy till age of 11, except for chicken-pox, tonsillitis, rheumatism in the hands, and a septic chin. At age of 11 fell on left knee and cut it. The wound began to fester and started "running up the leg"; opened over knee by patient's doctor; cleared up. Two months later patient had "hip disease" (right). As he had had rheumatism before in the hand, he thought that he had now the same trouble in the hip. The leg was drawn up and flexed; patient could only walk on the toes; not able to put heel down. Put to bed with extension weight of 7 lb., which straightened the hip; then placed in a Thomas splint. After the hip recovered, the right arm swelled up from the wrist to the shoulder. The doctor thought that this was a septic swelling, and came round next day to open it, but to his surprise the swelling had disappeared "like magic." It had only lasted for two or three days, and there was no discharge. Following this, various lumps began slowly to appear, beginning on the right hip. Patient noticed them by accident—feeling them under the skin—as there was no pain. At the same time the thighs began to become stiffer. The trouble then seemed to spread over the whole body, the limbs all felt tight, and the boy no longer had full freedom of movement. In 1928 he went to the Cardiff Royal Infirmary. One of the swellings was removed and diagnosed as "calcareous fibrositis." In 1930 a small sore appeared over the right hip and slowly spread. It discharged "pus" for three years, but is now soundly healed. (Actually it would appear that the initial discharge consisted of the typical milky fluid, which soon became secondarily infected.) Since then others have appeared in many places. He states that they dry up, and then break out somewhere else, especially when he has influenza or a cold. About a year ago a number of swellings, like a bunch of grapes, appeared in the right axilla; these disappeared with only a scanty discharge, and before this a large "threatening abscess" had developed in the left axilla, reaching as far as half-way to the elbow, and then receding spontaneously. He states that during the discharge from these different situations, "bits of flat yellowish pieces with jagged edges" used to come away; he thought these were pieces of bone.

I first saw him in November 1933, when his condition was as follows:—

Right arm.—Some wasting of muscles of arm and forearm; muscles rather more fibrous than normal. Several small subcutaneous nodules on forearm and immediately above elbow. Some redness over bony points of elbow; over one condyle remains of small sinus which is soundly healed.

Left arm.—Muscles rather more firm and fibrous than normal. Five small scars—remains of larger swellings—over anterior axilla; several small subcutaneous nodules over triceps.

Trunk.—Over cartilage of eighth rib, small nodule, which at one time discharged considerably. Over right iliac crest, large, irregularly shaped scar which had healed soundly; surrounded at lower extremity by subcutaneous nodules of varying size, and reaching into fascia of right thigh. Similar scar, but much smaller, over iliac crest. Attached to upper end of this is a flat plaque about 3 in. by 2 in. just under the skin.

Right leg.—Remains of large scar over right knee. Two scabs, of ordinary septic appearance, with a slight discharge, on posterior surface of leg. (These are apparently typical of the state of affairs when a sinus is discharging.) Very large scar, which has ceased to discharge—over the right trochanter. Popliteal and adductor tendons thickened and nodular.

Left leg.—Two small masses over tibia. Over left thigh, in front, several masses felt under skin, especially on outer side. Large scar over great trochanter, extending to buttocks. Both gluteal muscles rather firmer than normal. Remains of discharging scar on back of knee, popliteal and adductor tendons thickened and nodular. Hard flat thickened plaque occupies about two-thirds of posterior surface of thigh. When first seen, there was a cystic swelling at each end of this plaque, and a transmitted fluctuation could be felt between these swellings. With a needle 60 c.c. of milky fluid were removed. When patient saw this fluid he stated that the initial discharges from the other lesions had always been of this nature. The fluid had the following characters:—

It was sterile, and films of the sediment showed no cells.

Cholesterol content	...		189	mgm.	per	100	c.c.
Total N.	...	...	880	,,	,,	,,	,,
Na (as Na.)	...	...	325	,,	,,	,,	,,
K (as K)	...	...	15	,,	,,	,,	,,
Cl (as Cl)	...	...	348	,,	,,	,,	,,
Ca (as Ca)	...	...	580	,,	,,	,,	,,
P (as P)	...	...	260	,,	,,	,,	,,

$\frac{Ca}{P}$ ratio = 2·22 (which is the same ratio as is found in human bone).

Animal inoculation was negative.

The fluid was spectrographed by Mr. H. Ramage, of Norwich. The spectrogram showed very strong calcium lines, and the sodium lines were also unusually strong. The potassium and magnesium lines were weak, and the iron lines were just visible, indicating the presence of traces only. A trace of silver was also present.

Since its removal, the fluid has re-formed, and transmitted fluctuation can again be felt below the calcareous plaque—the two points of fluctuation being separated by a distance of six inches.

A nodule removed from the skin showed fibrous tissue only. Decalcified sections showed homogeneous material with no evidence of calcification or of inflammation.

Serum calcium (27.11.33)	12·2	mgm.	per	100	c.c.
,, ,, (28.11.33)	12·2	,,	,,	,,	,,
,, ,, (30.11.33)	14·6	,,	,,	,,	,,
Plasma phosphorus	2·2	,,	,,	,,	,,

A calcium balance on a low calcium diet containing 102 mgm. calcium oxide per diem gave an average daily excretion of 256·3 mgm., there being therefore a daily excess excretion of 154·3 mgm. calcium oxide.

Blood-count normal. X-rays showed numerous irregular deposits of calcified material; mainly in the fascial planes and subcutaneous tissues, especially in the thighs (figs. 1 and 2); in places these obscured the rest of the structure.

[I am indebted to Dr. Byrne-Quinn of Wolverhampton, with whom I first saw the case, Dr. G. E. Dyas, Honorary Radiologist, and to Dr. S. C. Dyke, Honorary Pathologist to the Royal Hospital, Wolverhampton, for their help with the investigations, and to Messrs. Ilford for their help in printing the X-ray plates, and to Dr. R. A. McCance, Biochemist to King's College Hospital, for his assistance in the chemical analysis of the fluid.]

Discussion.—Dr. PARKES WEBER agreed that this was an example of the rare generalized superficial "calcinosis," somewhat similar to the case he had demonstrated at the Seventeenth International Medical Congress (Dermatological Section), held in London in 1913. His patient was a little girl, and the calcareous deposits were becoming distinctly less, when the parents left England some time afterwards; the case was therefore lost sight of. A remarkable feature of the present case was the presence of fluctuating subcutaneous "lymph-sacs"—or as one might call them, "lymph-cushions"[1]—notably at the backs of the thighs.

FIG. 1.

Dr. HALLS DALLY agreed with Dr. Parkes Weber's conclusion that the fluid contained in the large fluctuating swelling on the posterior aspect of the left thigh was probably lymph, with considerable increase above normal of the calcium and cholesterol content. This elongated cyst, in the wall of which a large hard plaque was palpable, was apparently

[1] In regard to this formation of "lymph-sacs" *see* E. Kuznitzky and E. Melchior, "Subcutane Lymphsackbildung und Kalkablagerungen," *Arch. f. Derm. und Syph.*, 1916, cxxiii, p. 133.

superficial to the deep fascia, and in common with the swellings of similar character previously observed, was considered to represent dilated lymph spaces in the connective tissue.

POSTSCRIPT.—The patient in the case to which Dr. Parkes Weber had referred, a man aged 20, with absence of subcutaneous fat, had a calcareous deposit in the subcutaneous tissue of the elbow. When a local anæsthetic was injected in order to remove it for biopsy, the needle entered an extensive free space under the skin, occupying most of the arm. Both surfaces of this had a fascia-like sheen, and the authors compare the appearance to that seen on opening the dorsal lymph-sac of the frog.

FIG. 2.

This observation would explain, so far as the present patient is concerned: (1) the large collection of fluid in the subcutaneous tumour of the thigh, and (2) the history of periodic and often evanescent swellings—which might affect the whole of one segment of a limb. It is difficult to explain this feature of the history except on the assumption that a similar condition of "lymph-sac formation" in the subcutaneous tissues was present. This feature should be looked for in future cases of calcinosis.

Calcification in Raynaud's Disease.—R. MILNES WALKER, M.S. (introduced by Dr. J. H. SHELDON).

M. B., a girl, aged 14, four years ago consulted a doctor because of "gatherings" of her finger tips; the doctor noticed blue discoloration of the fingers and diagnosed Raynaud's disease. After treatment with ultra-violet light the "gatherings" cleared up.

Since then patient has noticed blueness of fingers in cold weather each winter, attacks of discoloration usually lasting about ten minutes; there has been no pain. Six months ago the "gatherings" recurred and have continued since then.

On examination.—Finger tips on both hands, palms of hands, and left wrist showed areas of calcification in subcutaneous tissues, the skin over some of these nodules being thinned; in places the nodules had actually ulcerated through the skin, and granules of gritty material escaped. Similar calcareous nodules could be seen beneath the skin of the under-surface of the left big toe and right fourth toe.

Calcification in Raynaud's Disease.

On three or four occasions the fingers have presented bluish discoloration like that in Raynaud's disease, but this has never been observed in the toes. On one occasion the left big toe presented a dead white appearance, but this passed off again in a few minutes.

X-ray examination reveals no bony abnormality in hands or feet. Calcareous deposits occur in subcutaneous tissues of most fingers, at left wrist, in left big toe and right fourth toe. X-ray examination of remainder of limbs reveals no further calcareous deposits.

Blood calcium 12·8 mgm.%.

[I wish to thank Drs. S. C. Dyke and G. E. Dyas for the pathological and radiological investigations respectively.]

Discussion.—Dr. PARKES WEBER said that this case was very similar to that of calcification in the hands of a woman with sclerodactylia described by Dr. R. E. Scholefield and himself in the *British Journal of Dermatology* (1911, xxiii, pp. 276-281). Raynaud's symptoms usually preceded or accompanied the onset of sclerodactylia and Dr. Walker's case (he suggested) already showed slight changes of sclerodactylia, together with the Raynaud features. Sir Thomas Lewis had suggested that the angiospastic attacks in question might be causally connected with the onset of sclerodactylia; and by others it had been suggested that the ischæmia from the angiospastic attacks might favour the onset of calcification in the fingers, just as conversely hyperæmia apparently favoured decalcification of bone (*cf.* the writings on the subject by D. M. Greig, R. W. Jones, R. E. Roberts, etc.).

Dr. CARNEGIE DICKSON said that the *British Medical Journal*, 1934 (i), 235, contained a paper by his colleague, Mr. J. Paterson Ross, entitled "Hypodermolithiasis," illustrated by a skiagram showing three examples of the condition in this case. In view of what Dr. Parkes Weber had just said in connexion with the contraction of the vessels from the action of cold, it was interesting to note that the first case in Mr. Paterson Ross's paper was one of a dispenser in whom an attack of "dead fingers" was liable to come on when she handled large cold bottles.

Infantile Scurvy (Barlow's Disease).—A. ROCYN JONES, F.R.C.S.

M. K., a boy, aged 12 months, was perfectly well until the age of 8 months, when, following an indefinite injury, the left lower limb began to be painful, and the child unwell. He weighed 7 lb. at birth and was breast-fed for one month, but this

FIG. 1.

way of feeding had to be discontinued because of the mother's illness. From that time onwards the diet was composed almost entirely of proprietary foods, the bulk of which consisted of condensed milk. The only fresh items were bread and butter given at 9 a.m., and fish occasionally. Orange juice was tried, but it appeared to induce vomiting on the few occasions when it was given; so it was dropped.

When admitted to the Orthopædic Hospital on December 7, 1933, the child looked very ill, and the skin of the face had a pale yellow tinge.

The whole of the left lower limb was very swollen (fig. 1), and acutely tender to touch; the child screamed at any sign of an intention to examine this limb. According to the mother, he was naturally contented, but the illness had made him very irritable. On gentle palpation the shafts of the femur and tibia were felt

FIG. 2.

to be distinctly swollen, but movements of the hip, knee and ankle joints were quite free and apparently painless; the bones alone were tender. No other limbs were affected except the wrists where there was some enlargement of the radial epiphyses. The mouth was clean, but the gums were spongy and there were submucous hæmorrhages, one of which, on the lower jaw, formed a prominent projection. There were no abnormal signs in the abdomen. There was a trace of albumin in the urine.

A skiagram of the left femur (fig. 2) shows stripping of the periosteum along the whole shaft, due presumably to hæmorrhage, and in the upper half of the tibia the peeling off of the periosteum is even more pronounced, due to greater hæmorrhage. The femoral epiphyseal line is increased and irregular, and is prolonged into a

spur-like formation on either side. It should be noted that there is none of the diaphyseal cupping so characteristic of pronounced rickets.

In view of the symptoms, signs and radiographic appearances a diagnosis of Barlow's disease was made, due to vitamin deficiency in the diet and particularly that of the antiscorbutic vitamin. The diet was therefore changed. Unboiled, undiluted certified first quality milk was given in the feeds—five feeds of 4 oz. each with one teaspoonful of brown sugar. The juice of two oranges a day was given between the feeds; this later was reduced to two teaspoonfuls in twenty-four hours. By the end of the first week the child began to lose his irritability, and the left lower

FIG. 3.

limb was much less tender. In the second week 3 minims of radiostoleum were added to each feed and a little tomato juice was given occasionally. The good progress continued until January 18, when an attack of bronchitis developed, but in a week this cleared up. It is now two months since the treatment began and all irritability has completely vanished; the child is contented and happy. The swelling of the left lower limb has largely disappeared and all the tenderness has gone, but there still remains some thickening of the shafts of the femur and tibia, due probably to calcification of the subperiosteal hæmorrhage.

A skiagram taken nearly five weeks after treatment started shows that calcification is proceeding in the subperiosteal hæmorrhages, and in the growing epiphyseal cartilages at the lower end of the femur and upper end of the tibia (fig. 3).

The temperature of the child during the first week varied between 99° F. and 101° F., and in the second week between 99° F. and 100° F.; and in the third week between 98·4° F. and 99° F.; the temperature rose during the bronchitic attack to over 103° F. but subsided afterwards to normal, at which it has remained ever since.

The diet has been increased and is now more varied—rusks with milk in the morning and, later, vegetable broth with greens, carrots and bread-crumbs.

[I am indebted to Dr. W. G. Oakley, M.R.C.P., for his help in the treatment, and to Mr. W. S. Dyson for his careful note-taking.]

The PRESIDENT said that in some cases of scurvy there was distinct loss of appetite, marked wasting and high temperature, and an erroneous diagnosis could easily be made if the history, defective supply of vitamin C, nature of the painful swellings and condition of the gums or palate were not properly gone into.

The swelling in a long bone such as the femur had sometimes been incorrectly diagnosed as osteomyelitis or tumour of the bone, while the position of the legs—which, on account of the attendant pain, the child refrained from moving—had, on a cursory examination, sometimes suggested infantile paralysis. He was glad that Mr. Rocyn Jones had called attention to the apparent calcification occurring in parts of large hæmorrhages. A skiagram in one of his (the President's) own cases showed the remains of the hæmorrhagic swelling of the femur after six months.

Ulcer in connexion with Keloidal Condition on Left Leg: Case for Diagnosis.—CHARLES E. KINDERSLEY, F.R.C.S.

R. S., aged 6. At birth a white line was noticed on the outer and posterior aspect of the left leg, extending from about half-way down thigh to the middle of calf. Some outlying marks also noticed at birth on outer aspect of foot. The mother states that there was no suggestion of the child being burnt. The middle of this area enlarged considerably and broke down, and has not healed since. Outlying thickened areas have appeared in connexion with the main mass, but the foot condition has remained almost unaltered. During the last six months there has been difficulty in walking, owing to contracture behind the popliteal space.

The leg appears to be normally developed and the mass seems confined to the skin and subcutaneous tissues. Sensations and reflexes normal. The hair in this area is long and fine (? owing to protection by a bandage). Wassermann reaction negative. Sections show no evidence of tuberculous infection. The child appears perfectly healthy and no other lesions can be found on the body.

Discussion.—Dr. PARKES WEBER said he thought that the case was one of linear sclerodermia, (zoniform morphœa),[1] which had become ulcerated. Sclerodermia of adult type had been known to have commenced before birth—an extremely rare occurrence—and he saw no reason why linear sclerodermia might not also be present at birth, though an example of the kind apparently had not yet been described.

Mr. A. H. MCINDOE said that a possible method of dealing with the leg was by applying a thick razor-graft to that portion of the ulcer on the posterior aspect of the calf, after complete excision of all scar tissue. As a preliminary to more radical and extensive treatment, this would, if successful, give information as to the behaviour of the keloidal element, and the advisability of further grafting. If it was unsuccessful, little harm would have been done to the patient, so that it was a justifiable experiment. At a later date an abdominal tubed pedicle could be transferred to the posterior aspect of the leg, replacing the entire area from the upper portion of the thigh to the knee. He did not think that X-ray treatment should be employed, in view of the obviously poor nutritional state of the tissues, and the danger of further damage to them.

[1] Dr. Parkes Weber's case of linear sclerodermia of the thigh was shown at the Clinical Section on May 2, 1913 (*Proc. Roy. Soc. Med.*, Clinical Section, vi, p. 213). The patient was a woman, aged 44, and the hard cicatricial band was considerably depressed. It had first shown itself at the age of 12 and had then reached its maximum development in about six years. After that it had remained stationary, or had even undergone slight involution. Cases in which the thigh is the part affected seem to be of extreme rarity.

Tumours of Jaws: Case for Diagnosis.—R. MILNES WALKER, M.S.

J. B., male, aged 25, a waggoner. First seen in October 1933. He stated that six years previously two teeth were extracted from the right lower jaw on account of toothache, and that the sockets had never completely filled in. He noticed nothing further abnormal until March 1933, when some teeth became loose; since then about half his teeth have fallen out; he visited hospital in order to have some more loose ones extracted.

On examination.—Only teeth remaining in upper jaw were incisors and canines, and two molars on right side. In the lower jaw, incisors, canines and first bicuspids on each side remained. Bicuspids somewhat loose. Upper and lower alveolar margins of both jaws in the parts from which teeth were absent had quite disappeared; the bodies of the jaws in those regions were covered by apparently healthy mucous membrane.

In the region of the right upper bicuspids was a deep ulcer invading both palate and cheek, the base being formed by a red granular surface. Similar ulcer in left upper molar region, but not invading palate. Both ulcers were spreading backwards into the pterygoid regions. Similar ulcers on outer aspects of lower jaws, in molar regions.

The body of the mandible was reduced to a thin strip of bone that felt quite firm, though the remaining alveolar processes were softened. No enlarged glands could be felt; no evidence of bony changes in other parts of the body. Slight pigmentation of the skin of cheeks and buttocks was noticed.

Pathological Investigations:—			mgm. %
Blood calcium:	October 19	...	10·5
	October 30	...	12·3
	November 10	...	11·6
Plasma phosphorus	...	...	5·7
Plasma phosphatase	...	...	3·7

Calcium balance: Calcium excretion exceeded calcium intake by approximately 380 mgm. per day, this being unchanged on normal and low calcium diets.

The following is a report on the microscopical examination of the margin of one of the ulcers, stained with hæmatoxylin and eosin:—

"Shows invasion of deeper tissues of the gum by neoplasm consisting of spheroidal cells with bulky cytoplasm and deeply staining nuclei, apparently a plasmocytoma."

Professor M. J. Stewart examined the microscopic slides and stained further sections with Pappenheim's stains, and reports:—

"There are any number of typical plasma cells giving beautiful carmine staining of the cytoplasm. The chief accumulations of these are round the periphery of the tumour mass, although there are also many in its interior, mainly in scattered patches. They are also very abundant in the œdematous corium away from the tumour, especially in the subepithelial zone, but there are also patches of the cells deeper down. The cells composing the tumour are larger than the plasma cells and much more irregular in form with large nuclei, often hyperchromatic, and showing numerous mitotic figures. In the main they are spheroidal, polygonal or ovoid in form, they do not give the slightest suggestion of typical Pappenheim staining of the cytoplasm and I do not even think that one can trace transition forms between them and the typical plasma cells which occur singly and in groups throughout the tumour. The van Gieson section shows a fine collagenous network throughout most of the tumour and in places the tumour cells lie in parallel rows as in plasmocytoma; this, however, is an inconspicuous feature.

"If this is a plasmocytoma it must be a much dedifferentiated one, such a process might account for the absence of typical Pappenheim staining and would be in keeping with the extraordinary absorptive and destructive action on the bone. Plasma-cell infiltration, as you no doubt know, is very frequent in all sorts of lesions about the mouth, syphilitic and otherwise, and even tumours may be invaded by such cells. Note, by the way, that there are a

Tumours of jaws. Right side.

Tumours of jaws. Left side.

considerable number of eosinophil cells also present in the tumour. In the Pappenheim section they stain a dark reddish brown as compared with the crisp carmine shade of the plasma cells."

A number of radiographic examinations were made and reported as follows :—

" Both sides of the mandible are very thin and have the appearance seen in the edentulous jaw of an old man. On the left side there is a localized area of bone rarefaction just in front of the angle of the jaw. In the superior maxilla on the right side there is a diffuse bone rarefaction in the position of the canine and bicuspids. The dental films show that the stump of the upper left bicuspid, the upper right lateral, canine and bicuspid and the lower left bicuspid and lower right canine all have the appearance of 'floating in space' and there is no true alveolus supporting them."

The patient has been treated by five weekly doses of X-rays, one-third pastille dose on each occasion (filter 3 mm. aluminium), and has also been taking calcium by mouth. The ulceration healed over very rapidly, two ulcers being healed before the X-ray treatment was started, and when the only treatment was oral hygiene and calcium by mouth.

The stump of the left upper bicuspid has fallen out, but the remaining teeth feel firmer in the jaw. A skiagram taken after the third dose of X-rays shows some regeneration of bone in the region of the angle of the jaw on the left side, but there is definite decalcification still going on in other parts of the jaws.

Wassermann and Kahn reactions negative.

[I am indebted to Mr. H. M. Browne, L.D.S., for bringing the case to my notice, to Dr. S. C. Dyke and Prof. M. J. Stewart for their pathological investigations, and to Dr. G. E. Dyas for the radiographic examinations and reports.]

(?) Diffuse Osteitis Fibrosa with Spontaneous Fracture of the Left Femur.—PHILIP TURNER, M.S.

Winifred P., aged 20, was first admitted to hospital under Dr. C. P. Symonds, March 10, 1928, on account of paraplegia and severe pain between the shoulders. Gradually increasing weakness of legs had been noticed for three months.

Condition on admission.—Complete anæsthesia below umbilicus; lower limbs spastic, completely powerless, but not wasted; knee- and ankle-jerks excessively brisk, plantar reflexes extensor; incontinence of urine. Wassermann reaction negative. Urine and cerebrospinal fluid normal. No abnormality of the vertebræ seen by X-rays.

Diagnosis.—Intramedullary lesion of the cord at the level of the 6th dorsal vertebra.

Treatment.—Deep X-ray therapy. After discharge patient stayed in bed one month and then gradually began to walk.

Readmitted 2.4.28, for further course of deep X-ray therapy. Improved considerably and able to walk fairly well. Improvement continued until August 1931, when she noticed progressive pain and weakness of left leg. Admitted February 1932 to St. George's Hospital, Ilford, where nothing wrong with the leg could be discovered. X-ray examination showed no abnormality of bones.

Discharged after eight weeks. Three days later had a spontaneous fracture of the left femur for which she was admitted to Guy's Hospital, under care of exhibitor. Radiologist's report stated that the upper part of the shaft of the left femur was infiltrated with secondary neoplastic deposit. There was a pathological fracture just below the trochanters. Later patient complained of pain in the left knee and right hip. Further X-ray examination showed similar bony changes in these regions. The serum calcium was 10·8 mgm. per 100 c.c. Blood-count normal. No tumour palpable in thyroid region. At first the fracture was treated in the usual way by extension, but as she was thin, anæmic, weak and ill she was allowed to go home in a plaster spica, after a further course of deep X-ray therapy.

Readmitted for further courses of deep X-ray therapy on 5.5.32 and 30.3.33. The serum calcium on each occasion was normal. Urine normal: no Bence-Jones protein present. She had not been allowed to stand since the accident for fear of another fracture, but the X-ray appearance was now so satisfactory that she was started on massage and commenced to walk again.

Since then she has been kept under observation. She walks well with a thick sole to the left shoe to compensate the shortening. She has put on flesh and looks well. There is firm union at the site of the fracture and the bones show no evidence of disease. There is no clinical or X-ray evidence of renal calculi, but there are two calcified masses on the right side in the pelvis. The serum-calcium test has been repeated and the result is still normal or slightly below normal. The thyroid region has been repeatedly examined, but nothing definitely abnormal has been found.

Mr. HAROLD EDWARDS: There are one or two features in this interesting case which make me doubt very much whether the diagnosis of osteitis fibrosa is correct. In the first place both the lesion in the spine and that in the bone responded to treatment by X-rays, and this common response to treatment is very strong evidence that both lesions are of a similar nature. As far as my experience goes, osteitis fibrosa is unaffected by X-rays, and is certainly not cured by them, and this fact is further evidence against the diagnosis given. Finally, although the skiagrams of the upper end of the femur show changes consistent with the diagnosis, the X-ray appearance of the lower end of the bone is quite different. The character of the lesion in the spine and the response to X-ray treatment suggest that myelomatosis is a more probable diagnosis.

Chronic Apical Tuberculosis treated by Upper Thoracoplasty.—H. P. NELSON, F.R.C.S.

Harry D., aged 40. Well until 1925, when he had hæmoptysis, and a diagnosis of tuberculosis was made. Treated in various sanatoria until August 1933, but no collapse therapy attempted during this time. On admission to Colindale Sanatorium in August 1933 he had a cough, and a trace of sputum which contained tubercle bacilli. On November 2, 1933, I performed thoracoplasty at Colindale, removing ribs 1 to 5—twenty-eight inches in all.

As the result of the operation the patient states that he feels much better in himself and is stronger; his appetite has improved, and he does not sweat as he did previously. Temperature, pulse and respiration normal; absolutely no sputum.

Pulmonary Tuberculosis with Cavity treated by Apicolysis.—H. P. NELSON, F.R.C.S.

William E., aged 19. In 1930 pains in the right side began and he had a cough. Treated with a right artificial pneumothorax; continued until October 1933, when he was admitted to the Brompton Hospital owing to spread of disease at the opposite apex, with a large cavity. The right artificial pneumothorax was abandoned, and a left one attempted but failed. Patient was therefore referred to me by Dr. Burrell for apicolysis. On January 2, 1934, this operation was performed through a posterior approach, resecting 1½ in. of the third rib. An extrapleural space was made in the apex of the left thoracic cavity by depressing the lung and this space was filled with 100 c.c. of paraffin wax. The wound was closed in layers.

A post-operative skiagram shows that the cavity has apparently been obliterated without interfering with the rest of the left lung.

Dr. PHILIP ELLMAN said that the advances made in thoracic surgery were of enormous benefit to physicians. It was now possible for the thoracic surgeon to perform thoracotomy as freely as the abdominal surgeon performed laparotomy. Surgical collapse of the lung and thoracoplasty in suitable cases, as instanced by the case shown by Mr. Nelson, produced astonishingly good results.

He was interested to learn that Mr. Nelson was not prejudiced against apicolysis, or, as he (the speaker) preferred to call it, extrapleural plombage, as many good results had been reported by continental workers. Technique was of considerable importance, the object being not to collapse the cavity mechanically by actual pressure, but to encourage its own natural tendency to retract. The case shown by Mr. Nelson was a case in point evidencing the good results obtained by proper technique. In carefully chosen cases, in which there was a localized cavity not larger than a small apple, and the general health was good, apicolysis was definitely indicated.

Pulmonary Tuberculosis with large Apical Cavity treated by Thoracoplasty.—H. P. NELSON, F.R.C.S.

William B., aged 18. Well until November 1930, when pain in left side of chest developed, with cough and sputum, which on examination was found to contain tubercle bacilli. Treated in various sanatoria until November 1932; then admitted to Colindale Sanatorium, where artificial pneumothorax was induced on the left side on account of a very large apical cavity (fig. 1); this was unsuccessful owing to adhesions. Sputum half an ounce daily; positive. Temperature occasionally 99°;

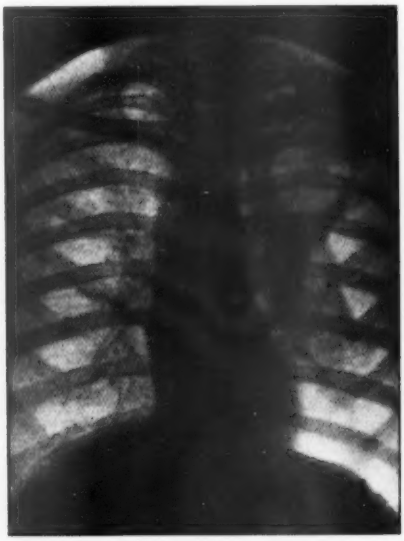


FIG. 1.—24.1.33. Showing extensive cavitation in left lung and artificial pneumothorax.

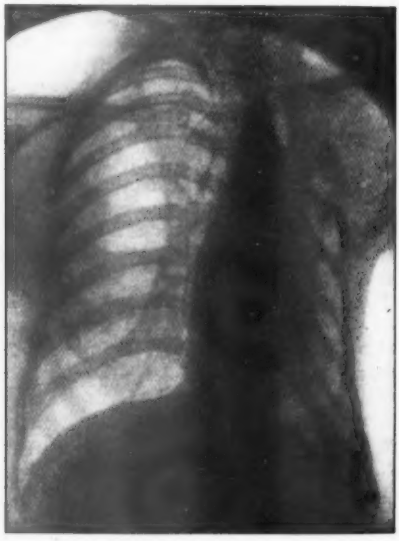


FIG. 2.—31.1.34. Showing collapse of chest wall obtained by complete thoracoplasty.

weight 9 stone. On May 9, 1933, I performed an upper thoracoplasty at Colindale, removing almost the whole of the upper six ribs. Two weeks later the second stage was performed, portions of ribs 7 to 10 being resected.

As a result of this operation there has been a remarkable improvement in the patient's general health; he is up and walking two miles a day; weight has increased, temperature, pulse and respiration are normal. There is half a dram of sputum a day; this contains a few tubercle bacilli. A skiagram shows that a cavity is still present, although only of minute size (fig. 2).

Reconstruction of Common Bile-duct.—C. E. SHATTOCK, M.S.

S. C., female, aged 48.

History.—Gall-bladder drained on account of empyema at hospital in country, January 1933. Drained for six weeks. No calculi. Gall-bladder removed at same hospital July 1933. Became jaundiced in September 1933. Stools clay-coloured, bile in urine. Jaundice varied in intensity but did not disappear. No jaundice previously.

December 1933. Examination. Obstructive jaundice of considerable intensity. No pyrexia. Patient thin and weak; confined to bed. Pre-operative treatment: glucose and intravenous calcium chloride.

Operation.—First part of the duodenum bound to liver by dense adhesions. Foramen of Winslow obliterated. Common bile-duct opened by separating adhesions between duodenum and liver. It was dilated and contained colourless "white" bile. The duct below this point was stenosed, and no bougie or probe could be passed into the duodenum.

Duct reconstructed by cutting flap of duodenum and suturing it over rubber tube passed upwards into proximal end of common duct and downwards into duodenum (A. J. Walton's operation). Owing to short length of duct exposed between liver and duodenum, the upper margin of the duodenal flap could not be sutured to the duct, but was sutured to the liver. Drainage tube inserted down to junction through stab-wound in loin.

Progress.—Bile drained for some days through stab-wound; became coloured on fourth day. Slight leakage of duodenal contents for one day. Jaundice disappeared. Stools became normal in colour. Bile disappeared from urine. Patient gained weight. The rubber tube in duct and duodenum does not appear to have been passed yet.

Mr. HAROLD EDWARDS said that he would like to congratulate Mr. Shattock on the extremely successful result in this case. No one who has not attempted these secondary—or, as in the present case, tertiary—operations upon the biliary tract can have any conception of the difficulties of the operation. Added to this, the subjects are for the most part jaundiced, and very bad operative risks. The case well illustrates the value of pre-operative treatment by intravenous calcium.

Precocious General Development of Normal Type in a Girl aged 14.—F. PARKES WEBER, M.D.

The patient (D. W.) will be aged 14 in a week's time, but looks more like a comely girl of 19 or 20. Her height is 168 cm., and she weighs 69½ kilograms. The mammæ are full and the pubic hair is abundant. A radiogram of the right hand and wrist (Dr. Franklin Wood) shows that the union of the epiphysis with the metaphysis has occurred in all the phalanges and is almost complete in the metacarpal bones. She has been troubled lately with multiple corn-like warts of the feet.

She is not only advanced in bodily development, but is said to be very intelligent and mentally well balanced. She is a rather big eater. She commenced to menstruate at 11½ years of age, and menstruation has been regular since then. For two or three years before the onset of menstruation she used to have short attacks of vomiting lasting about twenty-four hours and recurring on the average about once every month. When she was only four or five weeks old she seems to have had a bullous erythematous eruption followed by massive desquamation of some parts, especially of the hands, but she recovered completely within four or five weeks. She was not rachitic; she cut her first teeth at five months and walked at ten months. She had nocturnal enuresis till five years of age.

Brachial blood-pressure: 155/100 mm. Hg. The blood-count and urine show nothing abnormal. The blood-serum gives negative Wassermann and Meinicke reactions.

The patient is an only child. Some of her father's relatives were very big. Her mother is a woman of average size, in whom menstruation commenced at 15 years.

In regard to the possibility of early acromegalic gigantism, it should be noticed that (by radiographic examination) the pituitary fossa is well formed, but does not seem too large for the size of the patient's body; there is no hemianopia. It seems to me that the precocious development, as it affects all parts of the body alike (*cf.* Harvey Cushing's views on acromegaly), is most probably due to excess of the growth hormone produced by the eosinophil cells of the anterior part of the pituitary gland. Nevertheless, I regard the patient's general development as just within extreme normal limits. There is no sign of any abdominal or pelvic neoplasm by abdominal palpation. Over the hips there are a few small purplish cutaneous "striæ."

Recklinghausen's Neurofibromatosis, with Unilateral Buphthalmus and Multiple Changes in the Face and Skull.—F. PARKES WEBER, M.D., and O. B. BODE, M.D.

The patient, N. S., a man aged 32, has many typical "café-au-lait" pigmented patches and several bluish soft cutaneous tumours of neurofibromatosis scattered

FIG. 1.—*(Photograph by Dr. W. Gilges, 1934.)*

over his trunk and limbs. He is a "hunchback" with extreme dorsal kyphoscoliosis. The most remarkable changes are in his head, on the right side of which the soft parts hang down in a fold ("neurofibromatous dermatolysis"), including

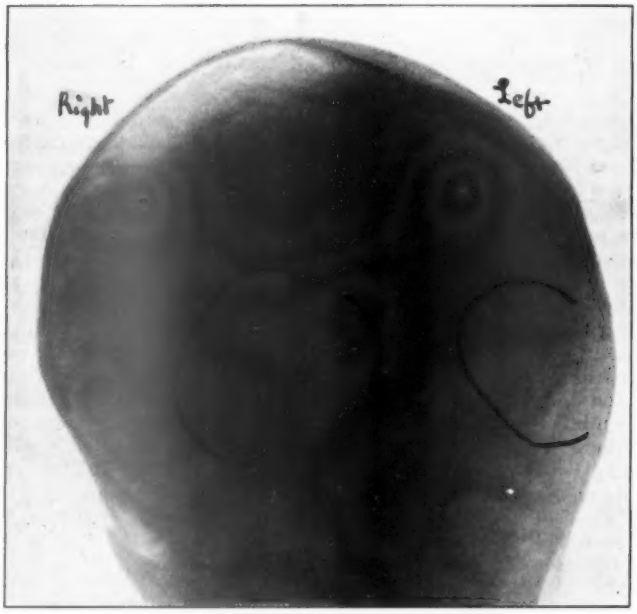


FIG. 2.—Antero-posterior skiagram of skull, taken slightly slantingly. For description see text.

FIG. 3.—Lateral skiagram of skull, showing especially the irregularity of bone at the back (see text).

a blind large eye (buphthalmus).[1] By ordinary and radiographic (Mr. Roth) examination the right orbit appears larger than the left; the right part of the skull-vault is bigger but thinner than the left. A bony mass projects on the right temple, just above the facial "dermatolysis." Above the occiput there is a vertical bony ridge with jagged prominences, and on the left of this ridge is a deep bony depression in the outer table of the skull. The pituitary fossa is long and boat-like, but without appearances of erosion. There are no signs of acromegaly. The patient's intelligence seems up to the average. His blood-serum gives negative Wassermann and Meinicke reactions.

According to the history the patient was quite normal at birth "like any other child." At 18 months he was dropped down some stairs. At 3 years he was becoming a "hunchback." At 4 years the right side of his face was noticed to be "falling" and dragging the right eye (which was increasing in size) with it. He has long been blind in the right eye, but up to the age of 12 years he could see well with it. There is no family history of any similar disease, and as there is no consanguinity between the patient's parents, the question of the case being a "first mutation" arises. In the combination of typical neurofibromatous features with bony changes the present patient, in a minor way, resembles the famous "elephant man" of Sir Frederick Treves.

A. Winkelbauer (*Deut. Zeitschr. f. Chir.*, 1927, ccv, pp. 230-257) discussed the cranial bone changes sometimes associated with neurofibromatosis, notably those accompanying elephantiasis-like conditions of one side of the face, as in the present patient. The chief changes that have been noted in the skull bones include: asymmetry between the two sides; thinning of bones and defective development; less often, thickening of bones. Not only the front parts, but likewise the posterior parts and the base of the skull, may be affected, as in the present patient; and enlargement of the pituitary fossa may be present quite independently of any change there may be in the pituitary gland itself (though acromegaly has been described accompanying neurofibromatosis).

Dr. CARNEGIE DICKSON said that with his colleagues, Dr. Worster-Drought and Dr. McMenemy, he was at present working up a case belonging to this group of diseases. In contrast with Dr. Parkes Weber and Dr. Bode's interesting case, their particular example showed an extraordinarily wide and varied distribution of fibroblastomatous tumours; for example, not only were there bilateral acoustic neurofibromata, but there were also innumerable smaller tumours upon practically all the cranial nerves and spinal roots, together with multiple meningiomatosis, vascular and other masses in the cerebral cortex, neurofibromata, gliomata, and ependymomata in the spinal cord, as well as minute microscopical tumours in the peripheral nerves, e.g. the sciatics, and also in the sympathetic ganglia, though not, as in some cases, in the gastro-intestinal tract, etc., or in the bones. In their case, only one subcutaneous tumour had been found, and this again was in marked contrast with Dr. Parkes Weber's case, and also with a case published in the current issue of the *British Medical Journal*. The condition, especially the meningiomatosis, had been described long previous to von Recklinghausen's account more especially of the subcutaneous tumours, not only in the famous Dublin case, but by Wishart, of Edinburgh, in the early part of last century. There were also even earlier, though less scientific, descriptions of the condition in the literature, e.g. that by Tilesius in the latter half of the eighteenth century.

Œdema: Milroy Type.—H. M. ODDY, M.B.

Miss L. C., aged 27. Swelling above left ankle began eight years ago, and swelling above right ankle two and a half years ago, with no apparent cause.

The only other symptom is aching in the legs and some increase in the swelling in hot weather, and after sitting in front of a hot fire.

Nothing of importance in the past history.

[1] In a buphthalmic eye from a case of neurofibromatosis Murdkami (1913) found more or less fibromatous involvement of all branches of the ciliary nerves within and without the eyeball (*cf.* J. H. Parsons, *Pathology of the Eye*, iii, p. 116).

Physical examination showed nothing abnormal, apart from œdema of both legs below the knees, with definite pitting on pressure.

Urine: no albumin. Urea concentration test was normal when patient was first seen a year ago.

Blood-count.—R.B.C. 5,420,000; W.B.C. 6,400; Hb. 104%.

In February 1933, œdema began in left hand, but no other parts have been affected. The degree of œdema has remained practically stationary, in spite of a prolonged course of massage.

Family history.—One sister, aged 31, had swelling of one foot, which began about eight months ago, and another sister, aged 16, has slight œdema of the left leg.

Dr. PARKES WEBER said he agreed in the diagnosis of the Milroy type of œdema. He thought that a very rare feature of the case was the involvement of one hand as well as of both lower limbs.

Carotid Pulsation (Resembling Aneurysm) in a Woman with Hypertension and Myxœdema.—E. STOLKIND, M.D.

A woman, aged 64, has been an out-patient under my observation for the last ten years, and suffers from anxiety psychoneurosis and myxœdema. I noticed hypertension (170 or more) eight years ago. Some years ago pulsation of both carotid arteries was noticed, but later the pulsation of the right carotid became more marked. The patient has had eleven children. There has been obesity for many years. Her hair is falling out and she is partly bald. She complains of general weakness. Wassermann reaction negative. X-ray examination shows very high diaphragm; aorta reaches to clavicle. Heart enlarged to left; sclerosis of aorta. Blood-pressure, taken recently, 235/135. The electro-cardiogram, for which I am obliged to Dr. John Parkinson, showed normal rhythm and slightly widened Q R S complex.

Left carotid artery, comparatively slightly pulsating.

In the right supraclavicular region up to the upper half of the sternocleidomastoid muscle there was a pulsating mass resembling aneurysm, which has increased during the last year. This pulsation of the right carotid is worrying the patient.

This is a case of myxœdema, sclerosis of the aorta, arteriosclerosis, cardiac hypertrophy with high blood-pressure; high diaphragm—with lifted aorta and its branches—and a right pulsating mass simulating aneurysm.

In other cases of mine with even higher blood-pressure there was no "kink" of the carotid artery nor was there such a kink in the case of another woman (demonstrated at this meeting) with blood-pressure of 260.

In the first case the aorta and innominate artery are pushed up, and as the upper end of the right carotid artery is more or less fixed, the lower part forms a "kink," and this "kinked carotid," when pulsating simulates aneurysm. The diagnosis is difficult. The degree of pulsation depends upon the position of the head. Such cases may be observed in men and women. No operation is indicated in this case.

Dr. J. F. HALLS DALLY said that this case did not conform to the pattern of bilateral and equal parotid pulsation, the dominant right-sided pulsation here being apparently conditioned by a pulsating mass (? aneurysmal dilatation), and by the right carotid being approximately a continuation of the axis of the ascending aorta, thus facilitating conduction of a more direct systolic shock.

There were two conditions, in the late stages of which bilateral and equal carotid pulsation in association with a high systolic pressure was of frequent occurrence; one was hyperthyroidism, and the other the arteriosclerotic form of aortic insufficiency. In both there was visible and palpable pulsatile dilatation of the carotids, a collapsing pulse and capillary

pulsation, as well as a raised maximal arterial pressure, the minimal pressure remaining at a normal level, in contrast with the endocarditic form of aortic insufficiency in which the minimal pressure was usually low. Carotid pulsation was best observed in the erect posture, an important point of differentiation from venous pulsation, which was best seen in the recumbent posture and disappeared or diminished in the erect posture.

Hemiatrophy of the Face (Unilateral Lipodystrophy). Condition improved by Insertion of Fat Grafts. — Sir HAROLD GILLIES, C.B.E., F.R.C.S. (Shown by A. H. MCINDOE, F.R.C.S.)

Mrs. E., aged 32. Resident of Johannesburg.

History.—In 1917 when aged 17, a small white mark appeared in front of the right ear, accompanied by pigmentation of the side of the face, and slight retraction of the upper lip. No wasting, no pain. Tonic and massage prescribed. For the next five years there was slow atrophy of the right side of the face.

31.1.33.

5.2.34.

1922.—Face badly sunken, especially above and below the zygoma. Found to have impacted wisdom teeth ; in 1923 these were removed with loss of bone. Patient was under Dr. Green Brinton (Johannesburg) for massage and electrical treatment.

In 1923 Mr. Bayers inserted a skin graft in both upper and lower sulcus to enable the patient to wear dentures.

22.12.33.—First seen by me. *Condition on examination*: Strong healthy-looking woman. Face : total atrophy of fat and subcutaneous tissue on the right side, leaving muscles and skin stranded out on bony framework. Zygoma prominent, with hollows above and below. Lip retracted upwards. Sensations normal. Motor

functions normal. Mouth: right half, upper and lower, edentulous. Glands normal, parotid secreting.

Diagnosis.—Localized lipodystrophy, with hemiatrophy of the face. Family history negative.

24.1.33.—Insertion of fat graft above and below zygoma, fat being taken from abdomen. Lower graft, result satisfactory. Upper graft, accidentally removed during expression of hæmatoma.

9.5.33.—Insertion of fat graft below mandible. Result satisfactory. Patient seen by Mr. Kelsey Fry for fitting of dentures.

21.9.33.—On examination, the fat graft was found to have consolidated into a tumour, causing a hollow in the malar-zygomatic region. Second hollow in region of chin scar.

3.10.33.—Insertion of fat graft through temporal incision over the malar and zygoma. Re-arrangement of chin scar.

Patient sent to Mr. Kelsey Fry for final fitting of dentures.

Note.—During the last year patient has gained much weight.

Hæmolytic Acholuric Jaundice with Splenomegaly and Normal Erythrocyte Fragility treated by Splenectomy.—TERENCE EAST, M.D.

Female, aged 46. Health first affected in December 1930.

Complained of abdominal pain chiefly in the left side, and vomiting. Jaundice was present for the first time. The spleen was found to be much enlarged. At this time the urine contained bile-pigments. The Wassermann reaction was negative. Bile was present in the fæces. Hæmolysis of red cells began at 0·45% saline and was complete at 0·35%. Between December 1930 and August 1933 considerable variation in the size of the spleen was noted.

Observations are tabulated below.

	R.B.C. millions	Hb. %	C.I.	Reticulocytes %	van den Bergh Units indirect	Fragility
6.12.30	4·0	80	1	2 normoblasts	42 (direct)	
16.12.30					42 (direct)	
6.1.31	3·8	76	1		12 (direct)	
22.1.31						normal
31.1.31					7 (direct)	
17.3.31					4 (direct)	
During this time there was some obstructive jaundice and bile was constantly present in the urine, but never absent from the fæces. The spleen decreased in size. Bile disappeared from the urine in April 1931.						
1.5.31					6	
Patient was better until the early part of 1932.						
20.3.32					3·8	
20.5.32					3	
Spleen hardly palpable.						
20.6.33					3·2	
15.8.33	3·4	73	1·05	9·2	0·7	
28.8.33	Splenectomy.					
30.8.33					3·5	
7.9.33	3·8	80	1·05	8·4	0·3	
11.9.33	Normal fragility of red cells.					

The spleen was removed by Mr. Arthur Edmunds. It weighed 37 oz. and was abnormally firm. Trabeculæ not increased; Malpighian bodies obscured. Colour, deep red. No free iron could be demonstrated. Microscopical section showed hyperplasia of the pulp.

The liver and gall-bladder appeared to be normal.

The patient made a rapid recovery, and during the last eighteen months she has felt much better.

Comment.—This is a case of jaundice, hæmolytic in character, due to hyperactivity of the spleen. In this instance there is no family history and the disease appeared fairly late in life. There was the usual tendency to secondary anæmia and the usual reticulocytosis. The intensity of the disease varied. Removal of the spleen has caused improvement. The phase of obstructive jaundice may have been due to the presence of biliary sand resulting from the excessive liberation of bile-pigment.

It is noteworthy that the red cells were not excessively fragile on the usual test with saline. A normal fragility may be present in these sporadic cases and also in those with familial incidence.

Section of Urology

President—A. Clifford Morson, O.B.E., F.R.C.S.

[*January* 25, 1934]

DISCUSSION ON THE FACTORS WHICH INFLUENCE RENAL FUNCTION AND THE VARIOUS METHODS OF INVESTIGATION

Dr. T. Izod Bennett (Abstract): Of the factors influencing renal function, the first to be considered is that of permanent anatomical change in the kidney, seen in a large group of diseases ranging from congenital abnormalities to nephritis of all types, malignant change, etc. The term "chronic interstitial nephritis" should be banished from medical nomenclature, the majority of physicians and pathologists being to-day agreed that "ischæmic nephritis" is the more desirable term, implying that the renal sclerosis is only part of the general vascular change. In only a small percentage of such cases the patients die from uræmia, although all cases of prolonged hypertension exhibit sclerotic kidneys at autopsy. Cases frequently occur in which marked elevation of the blood-pressure warns the physician that the kidney is only part of the picture, and urologists would do well to make examination of the blood-pressure part of their routine when examining cases. Death from cardiac failure or from a cerebral disaster may occur through ignoring the presence of this condition.

Complete suppression of urine occasionally follows the passage of instruments for relieving retention of urine or for the purpose of examining the lower urinary tract; such disasters are probably the result of a reflex ischæmia.

Changes in the quality of the blood reaching the kidney, as opposed to diminution in the normal volume of the blood supply are even commoner causes of renal insufficiency. Bacterial toxins following infections, and chemical poisons of known or unknown origin are examples. Diminishing renal function produces profound changes in the blood chemistry, these changes being more in the nature of alteration in proportion of the normal constituents of the blood than in the appearance of new chemical substances. But it is to be noted that changes in the chemistry of the blood may be the cause as well as the effect of alterations in renal function. Nitrogen retention of extra-renal origin is becoming recognized as less rare than has been supposed. The vomiting of acid gastric contents, intestinal obstruction, and alkalosis are amongst the recognized causes of this condition. Recent French observations indicate that in all these cases the important factor is oliguria; if for any reason the water supply to the kidney is reduced, nitrogen retention will tend

to occur, and if the kidney is already somewhat impaired in function, nitrogen retention may become severe and dangerous. Indiscriminate salt-free diets, or a high protein diet with a low fluid intake are causes to be borne in mind.

Suppression of urine following abdominal operations is one of the dreaded catastrophies of surgery; these cases are probably due in a large measure to nitrogen retention of the type just mentioned.

Obstruction in the lower urinary tract, a most important cause of renal impairment, is essentially the province of the urologist, to whom the profession owe most of their knowledge of the subject.

I am deliberately leaving discussion of such valuable methods of investigating renal function as cystoscopy and pyelography to my surgical colleagues. The best medical methods of investigating renal function consist in blood analysis and examination of the capacity of the kidney to secrete urine in full amounts and in appropriate concentration. The water tests of Volhard and Maclean's urea-concentration test are valuable methods of studying the latter factor, whilst Ambard's Quotient has long been utilized on the Continent and is of the greatest value, in that it depends upon the correlation of the concentration of urea in the blood, the concentration of urea in the urine, and the volume of urine secreted in a given time. This method has recently been modified and is being extensively used in London now in the form of the urea-clearance test of Van Slyke. It is of great value, but clinicians should always remember that it only gives information as to the function of the kidneys at a particular moment and must be often repeated if a true estimate is to be obtained. It would be very regrettable if surgeons became accustomed to employ this test, and particularly the percentage figure given by it, to the exclusion of complete chemical study of the urine and particularly of the blood.

[Cases were quoted showing the valuable information obtained by more complete blood analysis and illustrating the failure of this test to give reliable information in cases of nephrosis. Examples were shown of the rapid improvement exhibited by cases of acute nephritis when strictly treated and showing that the urea-clearance test made in such cases often gives misleading information in that it indicates a degree of recovery which clinical experience shows to be optimistic.

In conclusion, reference was made to a case in which old-standing trauma set up changes in one kidney resulting in months of pyrexia and ill-health without demonstrable changes in renal function. The patient was cured by nephrectomy and afforded an illustration of the dangers of relying exclusively on laboratory or local methods of examination.]

Mr. Duncan M. Morison: From a urological aspect, the majority of lesions which adversely affect renal function do so by producing some hindrance to the normal onflow of the urine. The hindrance induces on its proximal side a stasis, and soon there is established a state of back-pressure which is transmitted to the kidney, impairing its activity and ultimately leading to hydronephrosis. In addition to stasis there is the other important factor—infection. The two are closely related and tend to supervene the one on the other.

Omitting the more obvious lesions, I propose to review briefly certain forms of insidious obstruction. Broadly speaking, two main types occur in the urinary tract: (1) Primary. (2) Secondary.

In the primary group we have mainly a series of lesions due to developmental errors. In the other, the obstruction is a sclerotic process secondary to either direct infection or some source outside the urinary tract.

(1) *Primary obstructions.*—Throughout the conducting system, from the renal pelvis to the external meatus, there are sites at which the lumen normally presents a

localized encroachment, and it is at these sites that an excessive narrowing may occur (fig. 1).

From above downwards or proceeding distally, the sites are: (*a*) Pelvo-ureteral junction; (*b*) where the ureter crosses the iliac vessels; (*c*) at the broad ligament (in the female); (*d*) the ureteral opening within the bladder; (*e*) at the internal and external vesical sphincters; (*f*) the external meatus. Anomalies are also found within the posterior urethra, and congenital strictures in the penile urethra.

It is evident that an obstruction near the kidney will, as a rule, induce more rapid functional impairment than one more remotely situated. Exceptions occur, however, for even [with] a stenosis at the pelvo-ureteral junction efficient renal

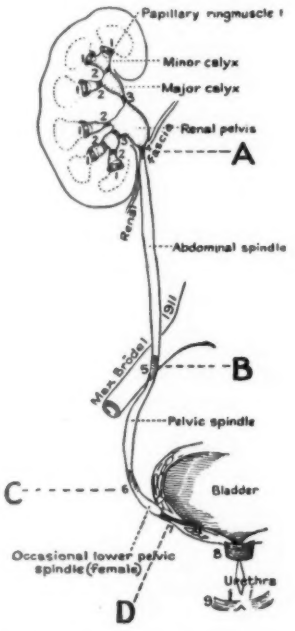


FIG. 1.—Normal sites of ureteric narrowings (Kelly and Burnam, vol. 1). A, pelvo-ureteral junction; B, where ureter crosses iliac vessels; C, broad ligament zone; D, transvesical portion.

function may persist for a considerable time if the renal pelvis is of the extra-renal type. In such instances the unsupported pelvic walls absorb the force of back-pressure by expanding, and thus delay parenchymal involvement. The obstructing factor here, as well as in the lower zones of the ureter, is usually a marked attenuation of the lumen without any increase of the mural constituents.

Divergence of opinion exists as to the nature of the lesion in the transvesical portion of the ureter. Is it a simple stenosis, an angulation, or, excluding these, purely an atony of the proximal ureter? A study of the condition in the light of analogy would tend to the impression of a primary stenosis followed by dilatation and, subsequently, angulation. Whatever the exact ætiology may be, these lesions are apt to induce marked ureteral dilatation with early renal failure.

The ureteral opening within the bladder may present a stenosis of its mucosal portion, constituting a ureterocele. Despite the flexibility of this mucosal obstruction, grave proximal stasis is frequently an accompaniment.

At the internal vesical sphincter or bladder-neck, a thin annular encroachment, due chiefly to the mucosal elements, is occasionally met with. This being a congenital lesion, the urinary symptoms are accepted by the individual as simply a personal idiosyncrasy, and it is only with the advent of failing health that help is sought, a distended bladder found, and the true underlying cause determined. It is probably in this type of bladder-neck obstruction that the prostatic electrotome achieves greatest success.

A somewhat similar form of obstruction is met with in the region of the triangular ligament, producing almost identical symptomatology, and as grave ultimate back-pressure.

Congenital urethral strictures differ from the acquired variety in responding more readily to dilatation. Meatal atresia, though anatomically furthest removed from the kidney, may prove a very definite factor.

All these lesions, by impeding the normal onflow of urine, produce proximal strain in which systole gradually gives way to diastole and the formation of stasis. Stasis, *per se*, does not appear to contribute mechanically to back-pressure, but aids in renal failure by encouraging and harbouring infection. Back-pressure is probably mainly due to the stimulus of proximal systolic action.

Apart from these purely mechanical obstructions, stasis may be produced by neuromuscular dysfunction, i.e. the "nerve-bladder" associated with spina bifida occulta, or in megalocolon where the lower urinary tract, more particularly on the left side, appears to share in the bowel changes. In support of this contention we have the beneficial results following presacral neurectomy.

Attention may only be drawn to the existence of some of these lesions when undertaking a routine urological examination, i.e. nocturnal enuresis, intractable bacilluria or pyuria, etc. In the absence of infection, a unilateral congenital ureteral lesion may achieve complete destruction of a kidney without giving rise to any local symptoms. Similarly, a bilateral lesion will silently impair renal function to such a degree that the actual cause is only detected after the onset of uræmic manifestations.

(2) *Secondary obstructive lesions*, following upon infection: (*a*) primary in the genito-urinary tract, or (*b*) secondary to some outside focus or general systemic cause.

This is a large group and one which is of particular interest to the urologist since, by anticipating and gradually overcoming the sclerotic process, renal impairment can be reduced, or kept in abeyance. I need not here enlarge on how repeated infection, or one that is retained where anatomically it cannot easily be evacuated, leads ultimately to the formation of fibrous tissue, which causes a loss of elasticity, and, by infiltration, impedes physiological muscular action. Of primary infections a typical example is the gonococcal, which is responsible for the production of urethral stricture, prostatitis, seminal vesiculitis, etc. The sequence of events which accompany urethral stricture are too well known to need repetition. The late effects which this infection produces, however, in relation to the male urinary tract, are apt not to be sufficiently appreciated. With chronic prostatitis and seminal vesiculitis there ensues a gradual fibrous-tissue infiltration of the bladder-floor and outlet, which interferes with the mechanism of urination, and leads to changes that induce lower ureteral embarrassment, and ultimately referred back-pressure on the kidneys.

In the female this form of direct infection plays a less important rôle as regards the urinary tract. There is, however, an acquired lesion in women which is of peculiar interest. It is commonly attributed to the trauma of childbirth, and

repeated attacks of cystitis. The findings in these cases show exactly the same bladder-picture as is present in chronic fibrous prostate, or median-bar formation. The symptomatology is at times remarkably similar in both sexes. The picture presented is of trigonal hypertrophy with accentuation of the inter-ureteric ridge, and approximation of this to the bladder-neck. The ridge, instead of being horizontal, is pulled down by the prolonged efforts of Bell's muscle into a U-shape. The transvesical portion of each ureter becomes compressed by the secondary hypertrophy of the trigonal and detrusor muscles. In addition to being compressed, this segment of the ureter frequently shares in the infiltrating fibrous changes which are present in the bladder-base, the resultant ureteritis giving rise to intermittent attacks of dull pain referred to the suprapubic region.

Infection due to intercurrent systemic upsets, e.g. influenza, typhoid and scarlet fevers, etc., or to some local focus, as teeth, tonsils, etc., may produce acute urinary infections, but probably more frequently insidious forms, i.e. prostatitis, and localized zones of ureteritis.

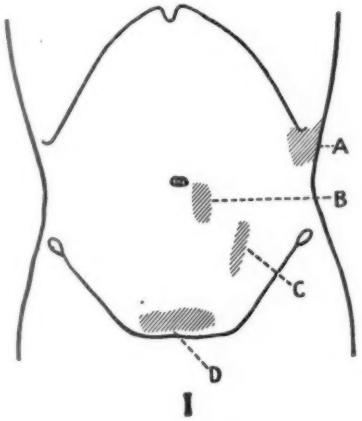


FIG. 2.—Approximate sites, based on clinical observation, to which pain is referred on the abdomen from various zones of ureteritis. A, pelvo-ureteral junction; B, where ureter crosses iliac vessels; C, broad ligament zone; D, transvesical portion.

Acquired ureteric lesions differ from the congenital, in that there is usually present intermittent pain in varying degrees (fig. 2). A ureteritis at the pelvo-ureteral junction gives rise to pain in the subcostal region; pain just below and lateral to the umbilicus indicates involvement of the ureteric node which lies over the iliac vessels. In the female a ureteritis at the broad ligament segment induces pain in the inguinal region. A suprapubic ache, as already indicated, suggests that the transvesical portion of the ureter is affected.

A ureteritis may be purely a zone of irritability, without diminution of lumen, which, on stimulation, enters into temporary spasm causing a block and back-pressure on the renal pelvis. In a well-established lesion there is a definite localized mechanical constriction, with proximal stasis and dilatation. At times a considerable length, or even the entire ureter, may be involved. Such ureters may show either marked diminution in calibre throughout, or a more or less uniform dilatation with apparent rigidity of the walls.

Bilateral ureteritis affecting the transvesical portion is very commonly associated

with bladder-neck obstructions. When it occurs independently it may be a cause of frequency and exertional incontinence in women, and of enuresis in the young.

Pathological conditions of the ureter, accordingly, play an important rôle as regards the functional activity of the kidney. Any departure from the normal process of adequately draining off all urine from the renal pelvis will initiate secretory difficulties for the kidney. A bilateral ureteritis throws an intermittent or mild continuous strain on the kidneys, which, in terms of impaired function is for a time so slight that the usual tests are inconclusive. Yet a careful study of the individual's symptomatology will reveal certain evidences of toxæmia—irritability, tiredness, loss of mental acumen, headaches, muddy complexion, gastro-intestinal upsets, etc., all of which tend to disappear on treatment of the ureteritis and promotion of better drainage. The causal condition in these cases is easily overlooked, since the urine is usually completely negative, and only in the transvesical type of ureteritis are there any bladder symptoms.

When infection does supervene on ureteritis it tends to become persistent, with exacerbations. Thus cases of chronic relapsing pyelitis are almost invariably the result of stasis, and it is essential in their treatment to correct by dilatation as far as possible any zones of ureteritis. Similarly, one of the ætiological factors in the production of calculi is stasis, and the more logical procedure is, first to institute a course of ureteral dilatation to improve drainage and minimize infection, before attempting to remove the calculus. The aim should be to render the field as surgically clean as possible before operation, as there is then less chance of subsequent stone formation.

Methods of investigation.—To obtain a proper estimation of the lower urinary tract, particularly the bladder-neck and posterior urethra, it is advisible to employ, both in children and in adults, a lateral as well as an end-view urethroscope. As all inspections in adults, and a large proportion in children, are carried out routinely under local anæsthesia, much information regarding the functioning of the bladder-base, bladder-neck, and posterior urethra can be elicited by observing the response to urination and noting the departure from the normal.

In studying the upper tract, it is customary first to employ small-sized whistle-tipped catheters (F4½—F5) in order to estimate the presence of any residual urine along the course of either ureter, or in either renal pelvis. During this procedure any ureteral hypersensitiveness or reproduction of previously experienced pain indicative of ureteritis is noted. An individual renal function test is now carried out. For simplicity coupled with sufficient reliability, an intravenous phenosulphonephthalein suggests itself, the time of appearance of the dye being noted on each side and thereafter adequate one or two period collections being made in order to estimate the percentage of dye excreted from either kidney.

For the determination of ureteritis it is essential to employ bulbed bougies, or catheters, the latter, advisedly, when a pelvo-ureteral site is suspected. By means of these "bulbs," the calibre, site and extent of a ureteritis can be estimated (fig. 3). The co-operation of the patient is important in confirming the findings, particularly as regards the type and location of discomfort produced, and whether it exactly simulates the pain complained of or not. For collateral evidence intravenous or retrograde uretero-pyelography is instructive, but, by comparison, does not afford the precision which bulbed bougies give in estimating ureteritis.

I have limited my remarks to a selected series of lesions that have one factor in common, i.e. obstruction, which by engendering stasis and back-pressure ultimately produces renal impairment. How is this achieved? I have already said that the resultant changes bring about hydronephrosis. The histology of the tubular and vascular alterations that occur are fully appreciated, but at the same time the physiological mechanism is obscure—and necessarily so, since the normal functional process is not yet evident. We know that the pelvic contents, even in a completely obstructed

hydronephrosis, are not stagnant, but are in a constant state of interchange. This may be due to tubular reabsorption once the papillary mucosal valves have been rendered incompetent. The process has been demonstrated both experimentally in animals and also clinically. A previously embarrassed kidney has remarkable powers of recovery within certain limits, but experimentally it has been shown that these limits are extended and a greater degree of recovery achieved if the opposite kidney is removed. It is accordingly somewhat difficult to define exactly what is recoverable impairment and what may be regarded as permanent impairment.

In studying urinary secretion in relation to hydronephrotic atrophy, the impression is gained that the most active function is carried on by the tubule systems situated

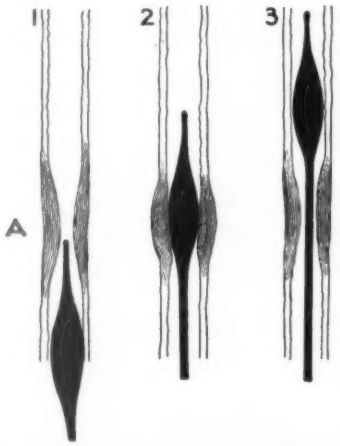


FIG. 3.—Diagrammatic representation of a zone of ureteritis being determined by the passage of a bulbed bougie. A, zone of ureteritis; 1, bulbed bougie approaching zone of ureteritis. No pain or resistance yet registered; 2, bulbed bougie passing through zone of ureteritis. Definite pain and resistance registered; 3, bulbed bougie has passed beyond zone of ureteritis. No pain or resistance registered. On the bulbed bougie being withdrawn the resistance and pain are again registered at the affected zone.

at the periphery of the cortex. The question may be raised, do the tubules situated at the various zones of the cortex possess a selective action? Is the renal tubule which is typified in textbooks the type which is common to all zones, or do those in the cortico-medullary zone become atrophic? In a human fœtus with only three layers deep of functioning glomeruli and tubule systems, urine has been obtained which showed all standard normal constituents. In the adult, however, if a hydronephrotic atrophy has progressed from the periphery centralwards till only three layers of glomeruli with their respective tubules are left functioning, we know that the urine secreted is definitely below the normal standard.

Dr. Cuthbert Dukes: The most useful contribution I can make to this discussion is to speak of those factors influencing renal function in which I have taken special interest, namely the effects produced by surgical operations, intestinal obstruction and urinary retention. The influence of these factors on renal function is well shown by daily observations with the Van Slyke urea-clearance test, which, as its name implies, measures the clearance of urea from the blood. With this renal-function test no urea is given by the mouth but the test is carried out whilst

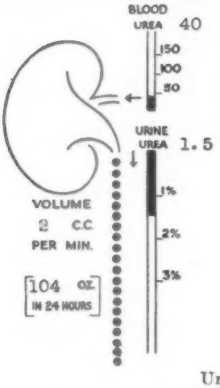
the patient is at rest under standard conditions (*see* Van Slyke and Peters' "Quantitative Clinical Chemistry," 1931). The rate of clearance of urea from the blood is calculated from the figures for the blood-urea, urine-urea and volume of urine excreted per minute. In one respect the tests to which I shall refer were not carried out strictly in accordance with the Van Slyke technique, because Van Slyke ascertains the rate of excretion of urine from the kidneys by measuring the volume of urine passed in two successive hours, and this proved an inconvenient method for the patients whom I have investigated, because of their inability to empty the bladder completely or to pass urine at the appointed time. My plan has been to collect the whole 24-hour specimen and to use this for estimation of urea and calculation of the average rate of excretion of urine per minute. This may not be a satisfactory method of performing the test on ambulatory subjects, but for patients confined to bed and properly nursed, it gave more reliable and consistent figures and was much less troublesome to all concerned.

Since urea-clearance is a comparatively recent arrival in the ranks of renal function tests, and one with which surgeons may not be familiar, I have tried to represent the information it gives in a pictorial manner (fig. 1). These drawings are intended to show the task with which the kidney is faced and the success with which it accomplishes it. The level of the blood-urea in milligrams per 100 c.c. is recorded in the upper scale, from which the arrow passes to the renal artery. The series of drops flowing from the ureter record the volume of urine passed per minute, each drop representing one-tenth of a cubic centimetre. (The volume is expressed also in ounces per twenty-four hours.) The scale beside this chain of drops records the percentage of urea in the urine.

Fig. 1 illustrates what is known as maximum clearance. Van Slyke has shown that when the volume of urine is large (over 2 c.c. per minute) urea excretion proceeds at maximum speeds, at such a pace as would clear 75 c.c. of blood each minute. This maximum urea-clearance is calculated from the formula $\frac{U}{B} \times V$, where U represents urea in urine, B urea in blood and V c.c. of urine excreted per minute. In the case depicted in fig. 1 the blood-urea was 40 mgm., the urea urine 1·5% and the rate of excretion 2 c.c. per minute. This would result in the clearance of 75 c.c. of blood each minute, and since this is the average normal the urea clearance is 100%.

When the rate of excretion of urine is less than 2 c.c. per minute (*see* fig. 2), the volume of blood cleared of urea decreases with diminished urine volume, the reduction being proportional to the square root of the volume of urine. The formula now to be used is $\frac{U}{B}\sqrt{V}$ = standard clearance. The mean normal level of standard clearance is 54 c.c. of blood per minute, compared with 75 c.c. maximum clearance, but neither of these figures need be remembered by the clinician, because the result in each case is expressed as a percentage of the normal.

Van Slyke regards urea-clearance as much the most sensitive test for renal damage and states that there is a 40% lowering of the standard or maximum figure when other tests are still within the range of normal variation. My own experience confirms this and I have illustrated in fig. 3 the difference revealed by the urea-clearance test in three patients each of whom had a blood-urea of 40 and a rate of excretion of ½ c.c. per minute. To clear 54 c.c. of blood per minute, the urine should contain 3% of urea. At first glance the urea excretion shown by the second and third patient is fairly satisfactory, but calculation shows the urea-clearance to be only 50 and 25% of normal. Thus considerable defects in renal function may be revealed by the urea-clearance test whilst the blood-urea is still within the normal limits.



Urea clearance
100% of normal.

FIG. 1.—Maximum urea clearance.

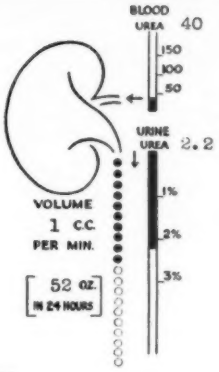
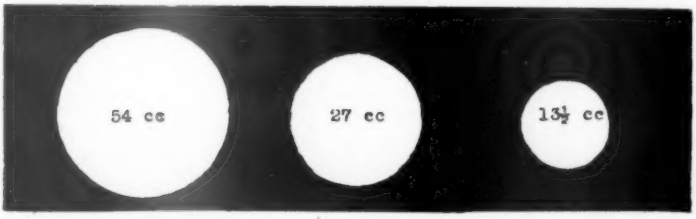
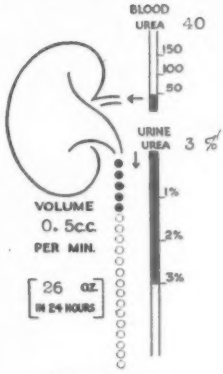
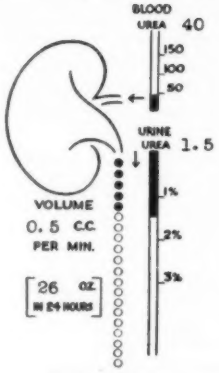


FIG. 2.—Standard urea clearance.

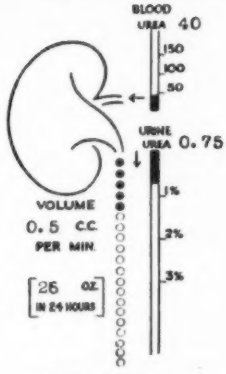




Urea clearance
100% of normal.



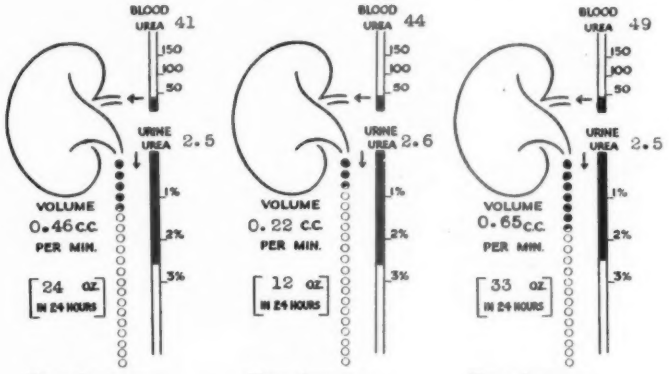
Urea clearance
50% of normal.



Urea clearance
25% of normal.

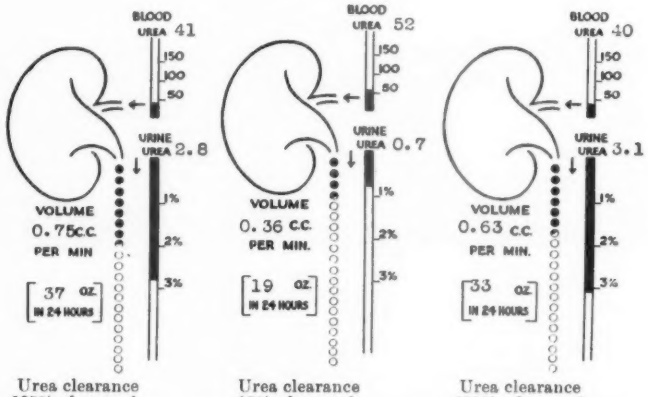
FIG. 3.—Defect in renal function shown by urea-clearance test whilst blood-urea and urine volumes are within normal limits.

Under standard conditions urea-clearance tests on the same individual give fairly constant results from day to day, the variation being in the region of about ten degrees. Much larger variations are brought about by change in diet and muscular exercise, but these rarely pass the wide limit of the normal range, which extends



Urea clearance 76% of normal. Urea clearance 52% of normal. Urea clearance 76% of normal.

FIG. 4.—Influence of minor surgical operation on renal function. Renal-function tests before and on two succeeding days after a minor surgical operation (excision of hæmorrhoids). On the day following operation, urea clearance fell from 76 to 52% but returned to the original level next day. (Male, aged 62. Lab. No. 4158.)



Urea clearance 105% of normal. Urea clearance 15% of normal. Urea clearance 115% of normal.

FIG. 5.—Influence of major surgical operation on renal-function tests. Renal-function tests before and on two succeeding days after a severe abdominal operation (excision of the rectum for cancer). A temporary decline in urea clearance was followed next day by a period of hyperfunction. The figures for the following days were 80%, 75%, 90%, 93%, 100%, 105%. (Male, aged 48. Lab. No. 4106.)

from 75 to 120%. Minor surgical operations under a general anæsthetic occasion a slight temporary decline in renal function, followed by recovery next day (fig. 4). More severe operations cause a greater temporary decrease in renal function (fig. 5). With improvement in the patient's general condition there may follow a period of

hyperfunction during which the kidneys compensate for arrears in the excretion of urea.

These two cases illustrate the course of events when all goes well. Some of the complications of surgical operations, however, particularly intestinal obstruction and urinary retention, may very seriously affect the behaviour of the kidneys. For instance, fig. 6 illustrates the renal-function tests in a patient who developed paralytic ileus after a serious abdominal operation (excision of the rectum for cancer) and who died from cardiac failure on the seventh day. The blood-urea rose steadily each day and the kidney made valiant efforts to excrete this excess with the fluid available, concentrating the urea in the urine on one day to more than 4%. The value of the urea-clearance test in distinguishing between intestinal obstruction and uræmia is well shown by this case, because even when the blood-urea had risen to 176, the urea-clearance test was only 8% lower than before operation. When, finally, the heart began to fail, the renal function steadily declined, as shown by decreasing volume of urine and less concentration of urea.

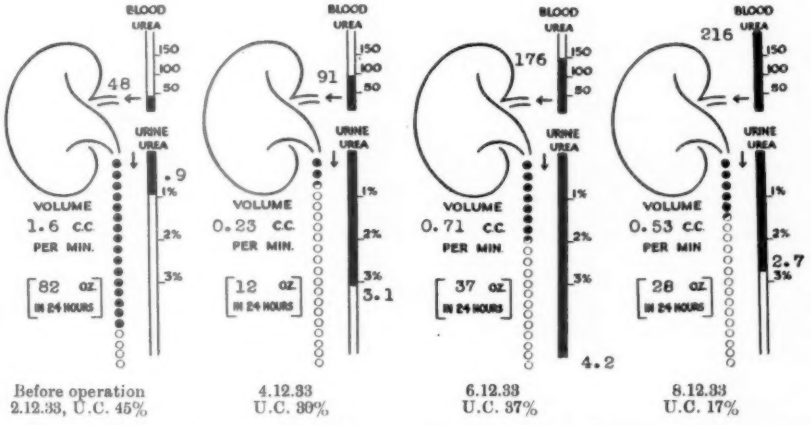


FIG. 6.—Influence of intestinal obstruction on renal-function tests. Urea-clearance tests before and after excision of the rectum for cancer. The patient developed paralytic ileus and died from cardiac failure on the seventh day. (Male, aged 66. Lab. No. 4230.)

The injurious effect on renal function of obstruction to the urinary passages is well known, although the rapidity with which this deterioration may set in is not always appreciated. Fig. 7 illustrates the effect of prostatic obstruction leading to partial retention and the quick recovery of renal function which followed replacement of an indwelling catheter.

The second part of the subject for discussion is the various methods of investigation of renal function. My contribution to this is a comparison of the blood-urea, urea-clearance, urea-concentration and urea-excretion tests in 100 cases of surgical disease of the urinary tract from St. Peter's Hospital. These four tests were carried out on each patient before operation, usually on the same day. For purpose of comparison, the response to these tests has been grouped into the categories "bad," "good," and "doubtful," according to the following standards. The blood-urea was classed as good when below 40, bad above 60, and doubtful from 40 to 60. The urea-clearance test was regarded as good above 75%, bad below 40%, and doubtful between. The urea-concentration test (MacLean) was

passed as good when any of the three-hourly specimens after the urea meal contained more than 2·5% urea, bad when none reached 2%, and doubtful between. When the volume passed in any hour was greater than 100 c.c. an adjustment was

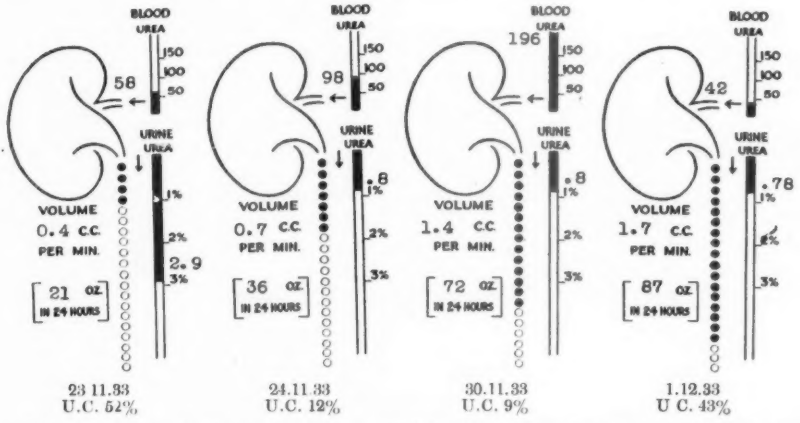


FIG. 7.—Influence of urinary infections on renal function. Case of urinary retention following excision of the rectum for cancer, 20.11.33, in a patient with prostatic obstruction. Indwelling catheter necessary for five days after rectal excision during which period urea clearance was 52% of normal. After removal of catheter the patient was not able to pass urine naturally and the blood-urea rose gradually to 196 mgm. and urea clearance fell to 9%. A catheter was tied in again on 30.11.33, and next day the blood-urea was 42 and the urea-clearance test was 43%. (Male, aged 72. Lab. No. 4175.)

made for this. The urea-excretion test was regarded as good when 10% of the ingested urea was excreted in two or more hourly specimens, bad when 10% was not excreted in any hour, and doubtful when 10% was only reached in one hour.

COMPARISON OF RESULTS OF BLOOD-UREA, UREA-CLEARANCE, UREA-CONCENTRATION AND UREA-EXCRETION TESTS IN 100 CASES OF SURGICAL DISEASES OF THE URINARY TRACT.

	Bad	Doubtful	Good
Blood-urea alone ...	26	48	26
Urea-clearance test ...	29	38	33
Urea-concentration ...	24	21	55
Urea-excretion ...	11	28	61

Using these standards, approximately the same number of patients would have been classed as "bad" by the blood-urea alone, urea-clearance and urea-concentration tests. Some of these, however, would have been passed as satisfactory by the urea-excretion test. It is not to be expected that the response to these four tests would be exactly alike, because each measures a different feature of renal activity. The figure for the blood-urea alone only shows whether or not there is nitrogenous retention. The urea-clearance test reveals the workaday function of the kidney under standard conditions of rest. The urea-concentration test measures the capacity of the kidney to rise to a special occasion and increase the concentration of urea in the urine. A good response in the urea-excretion test depends also on the reserve functional capacity of the kidney and is judged only by the quantity of urea excreted.

It is probable that one type of renal function test will prove most suitable for certain kidney diseases, and another type for other lesions. A clearer indication of

the most useful investigation to carry out in a particular case would often be of advantage. Evidence on such a question as this ought to be derived from as wide a circle as possible. My own experience with these renal function tests leads me to the conclusion that the estimation of the blood-urea gives more useful information than any other single test in surgical diseases of the urinary organs. In medical diseases, however, and in the intestinal complications of surgical operations, the urea-clearance test gives a much clearer picture of renal function.

Mr. Kenneth Watkins said that he had been much impressed with the value of the phenolsulphonephthalein test of renal function, which he had first studied in the Brady Urological Institute in Baltimore. The phthalein test had been introduced into clinical practice in 1910 by Rowntree and Geraghty of the Brady Institute. Later, after an investigation by Shaw of the same clinic, a fractional method was devised in which specimens were collected each half-hour after injection of the dye. This represented a considerable improvement in the clinical value of the test. Thomas, who had worked out a fractional method for indigo-carmine, recommended a fractional method for phenolsulphonephthalein in which the amount excreted in the first fifteen minutes was compared with that eliminated in the third fifteen-minute period following injection of the dye. [Mr. Watkins then showed some graphs of phthalein elimination made in cases of prostatic obstruction during the period of drainage.] In the normal, after the intravenous injection of 6 mgm. of phenolsulphonephthalein, the dye should appear in about three minutes, and a total of at least 70% should be eliminated in two hours. Considerably more than half of this should be excreted during the first half-hour. Defective renal function was shown by a delay in the appearance of the dye, and by a diminution in the total elimination over the two hours. Diminished function was also frequently shown by the fact that the greatest half-hour elimination occurred, not in the first, but in a later half-hour period, so that the peak of elimination seen in the graph was delayed to the second, or even later, period. In the graphs the recovery of renal function during drainage was shown by return to normal of the appearance time and of the total two-hour elimination, and by a return of the peak of elimination to the first half-hour period. (Some of the graphs shown were from Dr. Hugh H. Young's cases recorded in the *Journal of Urology*, 1931, xxvi, p. 25.)

Dr. Young and others had stressed the fact that it was of more importance to recover a maximal and stable renal function for each individual than to aim at a certain good level, as shown by the phthalein curve. Acting on this basis, Dr. Young had successfully operated on many cases with very poor function. For differential renal function this quantitative test provided much more information than the other tests at one's disposal. He (Mr. Watkins) was entirely convinced of the value of this test, which was so widely employed in American urological practice.

Mr. E. W. Riches said that he had been working for more than two years in conjunction with Dr. J. D. Robertson, using the urea-clearance test in surgical cases. After hearing what Dr. Izod Bennett had said, he thought the test must be of more value in surgical than in medical conditions. The clinical state of the patient was undoubtedly the most important consideration, but gave a reliable indication only at the extremes of good and bad renal function; all the border-line cases, between good and bad, required laboratory tests, and all prostatic cases certainly needed them at some stage. He had found the urea-clearance test the most trustworthy in this type of case, and would quote some examples in illustration.

A patient with a blood-urea of 32 mgm. %, and a urea-clearance of 52% died after one-stage prostatectomy. Another with a blood-urea of 38 and a clearance of 48%

died after endoscopic resection. Since these cases he had not operated on the prostate until the urea-clearance had been raised to 60% by drainage and other measures, and since taking this figure as the standard he had not lost a case after either prostatectomy or endoscopic resection. In another case the blood-urea was 56, and the urea-concentration 1·9% after two hours, but the urea-clearance was only 30%. This patient was drained by indwelling catheter, and subsequently by a suprapubic tube, but he died from uræmia having had no further operation. In a case of acute retention, with a severe infection, the blood-urea was never higher than 32, or lower than 25 mgm.% over a period of six months' suprapubic drainage, but during this time the urea-clearance rose from 34% to 68%. At this figure endoscopic resection was performed with confidence, and the patient made an excellent recovery.

In the surgical renal case the total function was not nearly so important in deciding for or against operation: a case of left renal tuberculosis had successfully undergone nephrectomy with a urea-clearance of only 33%, and eight months later the figure was 103%.

Three outstanding points which had arisen during the investigation were as follows: (1) If one kidney was absent or functionless, the urea-clearance might still be 100%; (2) after the removal of a tuberculous or pyonephrotic kidney the renal function tended to rise provided there was no secondary infection of the bladder or opposite kidney; (3) the presence of infection was the most potent single factor in depressing renal function.

Mr. H. P. Winsbury-White: There are often operative dangers in no way connected with a lack of skill in craftsmanship and not reflected in renal functional capacity. My object in emphasizing this is that we may remind ourselves of the necessity of maintaining a properly balanced view as to the place which renal function estimation has in urological surgery.

Renal functional tests are especially useful in showing a degree of renal incompetence which may never be suspected and cannot possibly be estimated clinically. For example it has been my experience that a patient with a blood-urea of between 300 and 400 may show no further clinical evidence of impaired kidney function than a patient whose blood-urea is about 80. And the importance of knowing the blood-urea reading lies in the fact that an operation on the former type of case is almost certain to be fatal.

I constantly make use of two types of bladder drainage—indwelling catheter and suprapubic cystostomy. Improved renal function is only one of the benefits which are generally manifested by this preliminary treatment. Even suprapubic cystostomy is a dangerous operation in certain cases of urinary tract disease, but by the proper use of the indwelling catheter this risk may be reduced very considerably.

In cases of prostatic obstruction, the effects of the obstruction may be so severe that not only prostatectomy, but also suprapubic cystostomy, is contra-indicated for the time being, and after even a prolonged period of indwelling catheter drainage it may be wisest to proceed no further, for a while, than the cystostomy. This process of coaxing back by stages an extremely debilitated patient to a state of health sufficiently good to justify prostatectomy, is reflected in the renal-function tests.

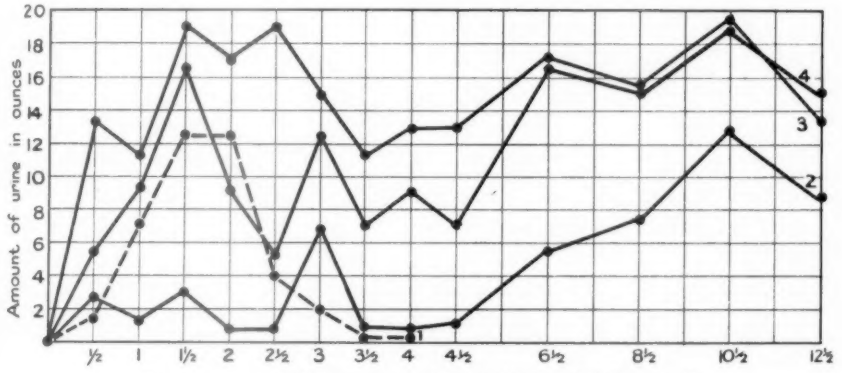
It has been my custom for several years to estimate the kidney function in cases of operation on the lower urinary tract, by (*a*) estimating the blood-urea percentage; (*b*) testing the renal capacity to excrete a given quantity of water; (*c*) testing the renal capacity to excrete the chemical substances in solution in the urine, by frequent estimations of its specific gravity.

Normally if a large quantity of water is drunk, a quick diuresis results. Most of the extra water is excreted within four hours, a greater part being eliminated in the first two hours than in the second. This test is especially useful when the

departure from the normal is only moderate, as the warning which it gives often precedes clinical evidence of renal failure.

Curve 1 on the accompanying chart gives a normal excretion measured at half-hourly intervals after drinking 50 ounces of water, within a space of half an hour.

Curves 2, 3 and 4 represent respectively the way the same quantity of water drunk in the same time was excreted by a patient aged 70 suffering from chronic prostatic retention at three different stages of his pre-prostatectomy treatment: Curve 2, just after commencing in-dwelling catheter treatment; Curve 3, after three weeks of in-dwelling catheter treatment; Curve 4, after four months of suprapubic cystostomy. It will be seen that each succeeding stage represents an increased capacity of the kidney to excrete water.



Figures on vertical lines = quantity of urine excreted (in ounces).
Figures on horizontal lines = half-hourly intervals.

With regard to the renal capacity to concentrate solids: Normally, after a meal there is first a drop in specific gravity as the water is excreted and not till three or four hours later does the specific gravity rise as a result of the excretion of the nitrogenous waste products of the meal. In prostatic cases this function is disorganized. The improvement in the renal capacity to concentrate after bladder drainage was reflected equally well in the case just referred to.

At commencement of bladder drainage: Five hours after 9 a.m. meal the specific gravity rose from 1002 to 1006.

After four months of bladder drainage: Five hours after 9 a.m. meal the specific gravity rose from 1010 to 1020.

Dr. George Graham said Dr. Izod Bennett had mentioned that the giving of large doses of alkalies could produce an alkalosis and so cause a patient with apparently healthy kidneys to develop uræmia. Alkalosis could be produced by severe vomiting, through the loss of hydrochloric acid and sodium chloride. The addition of alkalies might produce under this condition a dangerous degree of alkalosis, and so cause a rapid rise in the blood-urea. It was better to treat the vomiting with an intravenous injection of saline and glucose, together with small doses of insulin. Patients with a severe degree of nephritis were likely to develop acidosis and this again might cause a rapid increase of urea in the blood. The diagnosis could be made on clinical grounds, because a patient with acidosis often showed a condition resembling the air hunger of diabetic coma, with deep abdominal breathing, whereas

a patient with alkalosis had very shallow breathing. It was better to estimate the alkali reserve, as this enabled the observer to determine whether acid or alkali should be given, and also the correct dose.

He did not agree with Dr. Bennett that it was necessary to treat an acute nephritic condition with semi-starvation. All adult patients excreted at least 7 grm. of nitrogen each day when they were fasting, and it seemed better to give them a low protein diet with an adequate amount of carbohydrate and fat, because they would not excrete any more urea in the urine and would get the benefit of the food. He also thought that Dr. Bennett had taken too gloomy a view of the prognosis, because he had watched many patients with acute nephritis and a high blood-urea recover and keep well for years afterwards.

Section of Neurology

President—S. A. KINNIER WILSON, M.D.

CLINICAL MEETING HELD AT THE HOSPITAL FOR EPILEPSY AND PARALYSIS, MAIDA VALE, LONDON, ON JANUARY 18, 1934.

Bilateral Trigeminal Neuralgia, Paraplegia and Generalized Osteoporosis.—W. RUSSELL BRAIN, M.D.

Married woman, aged 59.

History.—1909: Gradual onset of weakness of arms and legs, especially on left side, reaching a maximum in a year.

1910: Admitted to London Hospital with spastic paraplegia, both plantars extensor. Since then, only able to walk about house with difficulty.

1926: Onset of trigeminal neuralgia on right side; all divisions affected.

1929: Onset of trigeminal neuralgia on left side in all divisions. Injections, (? of ganglia), about 1929, relieved pain on left side until three months ago, but had no effect on right side.

Nothing of note in previous or family history.

Present condition.—Mentality normal.

Fundi, visual fields, pupils and ocular movements normal.

Relative analgesia over second and third divisions of left trigeminal, following recent injection. Weakness of masticatory muscles on left. Bilateral weakness of lower face.

Upper limbs: Slight general muscular wasting; no fibrillation. Weakness more marked in left than right. No inco-ordination.

Lower limbs: spasticity and weakness more marked in left than in right.

Tendon reflexes: brisker on left than on right. Plantar reflexes: right flexor, left extensor. No sensory loss. Kyphoscoliosis. Heart, lungs and abdominal and pelvic viscera normal.

Radiograms of the bones show marked generalized osteoporosis, relatively more circumscribed in the cranium than in other bones. Blood Wassermann reaction negative. Blood-count normal.

Serum calcium – 8·6 mgm. per 100 c.c.; plasma phosphorus – 2·7 mgm.; plasma phosphatase – 0·328 mgm.

Cerebrospinal fluid.—Normal in all respects; Wassermann reaction negative.

Discussion.—Dr. RUSSELL BRAIN: One sees patients with trigeminal neuralgia on one or both sides and spastic paraplegia, and it is often thought to be due to disseminated sclerosis. This may be so in some cases, but I am not convinced that it is so in all, and I do not think that is the right diagnosis in this case.

The PRESIDENT said he regretted the absence of Dr. Wilfred Harris, as he was a protagonist of the view that cases of combined trigeminal neuralgia and paraplegia were really cases of disseminated sclerosis. There were cases in which, on post-mortem examination, that seemed to be the diagnosis, but he (the speaker) did not think all belonged to the group. When he was a house-physician at Queen Square Hospital, Sir Victor Horsley had operated upon a man whose case had been diagnosed by Sir William Gowers as one of spinal tumour. It was not a case of tumour but one of meningitis circumscripta, or, as Horsley termed it, meningeal cyst. He (the President) followed the case for many years. After the operation the patient had had mild compression paraplegia, and made a fair clinical recovery. Twelve years later he developed right trigeminal neuralgia, and three years after that he had left trigeminal neuralgia. It was now about 25 years since he, the speaker, first saw him, and he was still slightly paraplegic. He had never had any other signs except paraplegia. Dr. Wilfred Harris gave him injections for the trigeminal neuralgia. No doubt Dr. Harris would regard the case as one of disseminated sclerosis, but the history seemed to be definitely against that view. At the operation he (the President) had seen the arachnitis circumscripta adhesiva of the cord, which he did not think was a feature of disseminated sclerosis. Therefore he agreed with Dr. Brain that there were cases of this condition which did not belong pathologically to disseminated sclerosis.

Symmetrical Paralysis of Shoulder-girdle Muscles and Extensors of Wrists and Fingers, ? due to Lead.—W. RUSSELL BRAIN, M.D.

Barman, aged 39.

History.—August 1933 : Onset of progressive bilateral weakness of upper limbs, associated for the first few days with cramp-like pains. No other symptoms. No known exposure to lead, except that lead pipes are used for the beer on some occasions in the public house.

Since admission to hospital on December 1, there has been considerable improvement in the shoulder-girdle muscles.

Five years ago attacks of abdominal pain lasting a week on two occasions.

Present condition.—Slight bilateral weakness of facial movements, both upper and lower ; vocal cords move normally.

Trapezii and sternomastoids normal.

Wasting and weakness of all muscles of upper limbs, except flexors of fingers. Affected muscles, in order of severity ; deltoids, extensors of wrists and fingers, biceps, triceps, latissimus dorsi, pectoralis, small muscles of hands. Fibrillation not noted.

Tendon reflexes in upper limbs present, but sluggish ; supinator-jerks brisker than biceps and triceps jerks.

Electrical reactions : extensors of wrist right and left—no response to faradism, but response to galvanism at 10 m.a. All other muscles of shoulder, arm and hand respond to faradism.

No sensory loss. Rest of nervous system normal.

Blue line seen at gum margin, but the dental surgeon reports that this is due to tartar.

Blood-pressure 108/65. Heart, lungs and abdomen normal. Urine normal ; no lead found.

Blood : R.B.C. 4,700,000 ; Hb. 64% ; C.I. 0·68. No sign of punctate basophilia. Blood Wassermann reaction negative.

Cerebrospinal fluid.—Normal in all respects. Wassermann reaction negative.

The PRESIDENT said that some cases of lead palsy went on to amyotrophic lateral sclerosis, which, he thought, was not excluded in the present case, despite the fact that, for the time being, the patient seemed to be a little better. He had himself published similar cases : he had seen some which commenced as typical extensor palsy, with lead as the ætiological factor : and, in the fulness of time, they developed amyotrophic lateral sclerosis of the usual kind. In the present case there was no increase of reflexes : and if it was going to be of this clinical variety it was at present at too early a stage for decision.

Myelitis with Blindness : Acute Disseminated Encephalomyelitis.—DOUGLAS MCALPINE, M.D.

A. K., female, aged 22.

16.1.33.—" Influenza," cough, no sore throat.

20.1.33.—Pain across shoulders persisting several days.

26.1.33.—Tingling in left thigh spreading upwards to abdomen and downwards, and then to other leg ; complete in three days. Numbness followed.

27.1.33.—Weakness in legs. Retention of urine, lasting 40 hours.

30.1.33.—Admitted to Neurological Ward, Middlesex Hospital. Temperature normal. Highly intelligent patient. Cranial nerves and upper limbs normal. Paresis of lower intercostal and abdominal muscles, marked paresis of right leg ; moderate paresis of left leg. Abdominal reflexes absent. Left knee-jerk slightly increased ; right diminished. Ankle-jerks brisk. Plantar responses extensor. Flexion withdrawal reflex easily elicited below knees. All forms of sensation diminished on trunk below D.4. Tactile sensation unimpaired both legs. Thermal and pin-prick sensation retained below L.3 on right side, absent in left leg. Vibration

sense absent, and recognition of figures drawn on skin impossible both legs, yet postural sense all toes unimpaired. Retention of urine and incontinence of fæces.

Cerebrospinal fluid: Wassermann reaction negative; 4 cells per c.mm; protein 0·03%. Lange 1111222100.

3.2.33.—Both knee-jerks absent. Ankle-jerks brisk. Paresis of left leg more marked. Thermal and pin-prick sensation now lost in right leg. Postural sense still present. Signs of bronchitis.

6.2.33.—Paresis more marked lower limbs. Signs of collapse in lower lobe left lung.

Subsequent history.—By middle of February power of left leg much improved; still marked paresis of right leg. Knee-jerks feebly present, ankle-jerks still exaggerated; plantar responses extensor. Paradoxical response to cold tube in right leg, and in a few days thermal and pin-prick sensation returned in right leg and began to recover in left leg; by 28.2.33 these forms of sensation were normal on right side below level of lesion, but slightly impaired on left side. Vibration sense and recognition of figures impaired up till beginning of April. Postural sense remained normal throughout, except on two consecutive days. Sphincter control returned. Patient discharged on May 4 with a moderately severe spastic paraplegia.

Diagnosis.—Acute disseminated myelitis.

Improvement continued for one month, then patient noticed blurring of vision of right eye.

20.6.33.—Vision of both eyes rapidly failing, and three days later nearly complete blindness.

27.6.33.—Pain in stomach radiating through to back with recurrent vomiting.

29.6.33.—Legs weaker, and on following day loss of sphincter control.

3.7.33.—Readmitted to hospital. In addition to above, complaining of tingling in arms. Temperature 101° F. Both pupils dilated, slow response to light. Perception of light only. Veins full, otherwise no change in fundi. Remaining cranial nerves normal. No loss of power of upper limbs, or alteration in reflexes. Thermal and pain sensibility lost between C.6 and D.1 on both sides; other forms sensation normal. Complete paraplegia in extension with well-marked flexion reflex. Loss of all forms sensation below D.3.

5.7.33.—Frequent vomiting since admission. Loss of thermal and pain sensation now extends up to include C.4 on both sides. Slight weakness of both hand-grips.

6.7.33.—Arm reflexes absent, marked weakness of fingers of both hands, flexion of wrist, and to less extent extension of wrist and elbow. Flexion of elbows and abduction of shoulders unaffected.

7.7.33.—Thermal and pain sensation impaired up to C.3 on left side. Power now diminished at both elbows and slightly at shoulders. Postural sense slightly impaired right, more so left hand. Vibration sense completely lost.

8.7.33.—No further extension upwards of anæsthesia, but now complete loss of postural sense at all joints both arms. Diaphragm unaffected. Can count fingers right eye. Left eye, perception of light only.

Further progress.—Complete blindness developed with double optic atrophy. Power has partially returned in both arms, but to an insignificant extent in lower limbs which are now showing paraplegia in flexion. Thermal and pin-prick sensation impaired between C.5 and D.1 on right side, and below C.3 on left side. Tactile sensation practically normal. Complete postural loss fingers right hand, and impaired left hand. Vibration sense only slightly impaired. Appreciation of hot and cold and pin-prick lost below D.3 on right side. On left side these forms diminished below D.3. Nearly normal in sacral segments. Complete loss of postural and vibration sense of both feet. Incontinence of urine.

3.1.34.—Cerebrospinal fluid: Wassermann reaction negative; 5 cells per c.mm.; protein 0·03%. Lange curve normal.

Discussion.—Dr. McALPINE: The clinical picture in this case can be divided into two phases. The first began in the middle of January 1933 with catarrhal symptoms followed by pains in the trunk and a rapidly developing myelitis at the level of D. 4. Subsequently there was a slow and incomplete recovery. The points which suggested acute disseminated myelitis rather than disseminated sclerosis were (1) the pain at the commencement, (2) the condition of the reflexes in the lower limbs—namely loss of knee-jerks with brisk ankle-jerks and extensor plantar responses. A finding which is difficult to explain was the complete retention of postural sense in the toes while at the same time vibration sense and recognition of figures drawn on the skin were completely lost below D.4. I have never previously seen this posterior column dissociation in acute myelitis.

The second phase of the disease began in July, a month after the patient's discharge from hospital, with rapid failure of vision and signs of a fresh myelitis at the level of D.3. Of interest was a bilateral loss of thermal and pin-prick sensation between C.6 and D.1 on both sides. Other forms of sensation were normal for a few days; subsequently postural loss, etc., become profound with loss of power.

It is obvious that the lesion in the cervical region began in the centre of the cord and spread outwards and upwards. Other points are (1) persistent loss of postural sense in the hands and feet six months after the second relapse; (2) sparing of the lower sacral segments on the left side; (3) complete permanent blindness, both eyes.

I think these points rule out disseminated sclerosis. Is this a case of so-called neuromyelitis optica? There is nothing in the clinical picture which does not fit in with the diagnosis of this disease; in particular the cervical cord is often affected by a central area of necrosis. Blindness is said to be very rare.

A review of the literature, however, during the past ten years shows an unusual number of cases of bilateral retrobulbar neuritis with or without signs of myelitis. In most of these cases a mild papillœdema was present, and in the majority sight was restored partially or wholly. Most of the authors writing on this subject have classified these cases not as examples of neuromyelitis optica, but as forms of acute disseminated encephalomyelitis. This disease seems to have taken the place of epidemic encephalitis. Relapses are comparatively rare, but do occur, and I believe that the present case is an example of this disease in which the virus has remained active.

Dr. MACDONALD CRITCHLEY said he believed that in neurology there were two mythical maladies, and that one of them was neuro-optical myelitis. He thought the present case would be relegated to the category of disseminated encephalomyelitis, as Dr. McAlpine suggested.

The PRESIDENT asked whether any encephalitis was present. ["No, unless an affection of optic nerves."] He had asked the exhibitor whether he had observed hemianopic loss when the symptoms occurred. That would have been interesting, because the virus or agent, which could be called "x," passed up in funicular fashion. Some called the disease funicular myelopathy, an obscure set of words. The point was its funicular character, as if there were partitions in the cord, of which nothing was yet known. Why should a noxa go up the whole funiculus of motor cells and never spread beyond, leaving the lateral horn untouched, as well as the posterior? In the cases of the kind which he had seen there was very little spread to the chiasma, and there was a transient hemianopic defect before optic atrophy set in.

Spino-cerebellar Ataxy with Amyotrophy.—W. G. WYLLIE, M.D.

Alice M., aged 67, was normal up to the age of 49, when she commenced to have trembling of the hands, followed by weakness and dragging of the legs, hesitancy of speech, giddiness and wasting of the muscles of the hands and feet. The progression of the symptoms has been very gradual, and latterly there has been little change.

Family history.—Father died aged 88; had had shaky arms for many years, gradually becoming paralysed and bedridden, unable to raise his arms. Siblings: one brother and one sister, both dead; neither had any nervous complaint. Patient has two daughters, aged 39 and 38, both healthy; eldest has a healthy child aged 3 years.

Present state.—Unsteady ataxic, steppage gait, often falls. Marked intention tremor of hands. Trembling movements of lower jaw, most noticeable on speaking. Staccato speech. Slight titubation of head.

Optic discs normal. Pupils equal and react to light. Nystagmus usually absent, occasionally very slight on left lateral deviation. Other cranial nerves normal.

Arms.—Clawed hands with marked wasting of the intrinsic muscles, and some wasting of the forearms. Strength good at shoulder; poor distally. Marked intention tremor. Tendon-jerks absent.

Legs.—Drop-foot—bilateral. Knee- and ankle-jerks absent, plantar no response.

Sensory changes.—Slight diminution to light touch at the periphery of the extremities, and some impairment of joint sense and sense of position in the legs, also vibration cause reduced. No sphincter disturbance.

Intelligence.—Fair, rather facile; memory rather confused.

Discussion.—Dr. WYLLIE: The main points of interest in this case are the association of localized muscular atrophy with generalized ataxy, the almost synchronous onset of the two conditions, and their commencement late in life, i.e. at 49 years of age. I suppose there is no doubt that the condition belongs to the hereditary ataxias or hereditary degenerative conditions of the cord and cerebellum. There is a history of a similar complaint in the father, though the patient does not remember many details. As to the muscular atrophy being so localized to the periphery, I can find no record of similar cases in the literature, though muscular atrophy is mentioned as commencing at a late age. There is a familial or spastic condition with amyotrophy, with onset in childhood, and in which only the hands were affected. At an autopsy on such a case there was found to be degeneration of the pyramidal columns, the anterior horn cells, and the size of the cerebellum was small. In the present case one would expect that the spino-cerebellar tracts were affected, and the dorsal columns, with a local degeneration of anterior horn cells in the cervical and lumbar enlargements.

The PRESIDENT remarked that in the familial groups one could meet with many combinations: all sorts of family records had been published which did not fit in with any of the recognized schemata. The present case did not so fit. Cases had been recorded of aberrant Friedreich's disease, spino-cerebellar cases half-way between Friedreich's disease and hereditary cerebellar ataxia in which there was amyotrophy. The occurrence of this type of amyotrophy was of interest from another point of view, because some cases of syphilis showed this systematized combination: combined sclerosis, absent deep reflexes and posterio-lateral column symptoms, extensor response, and wasting of muscles.

Werdnig-Hoffmann's Disease.—W. G. WYLLIE, M.D.

D. M., male, aged 5 years and 9 months; born at full time, normal delivery; second of two children.

The mother states that at the age of 10 months the child could crawl but has never walked. When first examined about this time at the Hospital for Sick Children, Great Ormond Street, muscular weakness was noticeable at the proximal ends of the limbs. Beyond the fat covering the bones, very little muscle substance could be felt at the proximal ends of the limbs. The child had great difficulty in raising the arms at the shoulders, but with the elbows supported had full use of the hands and a good grasp. In intelligence the child has always been forward.

The progress of the disease has been very gradual, but latterly intercostal weakness has been observed. The child's power of coughing is feeble. Now there is some atrophy of the tongue. Scoliosis, contractures at the knees and ankles have occurred; the tendon reflexes are all absent.

The PRESIDENT said the tongue was now beginning to atrophy; it was dimpled and puckered a little. The case seemed to be a characteristic one of the condition.

Cerebral Abscess (Left Frontal Lobe) following Acute Infective Osteomyelitis of Frontal Bone.—CHARLES DONALD, F.R.C.S.

S. H., male, aged 13.

History. — Admitted to London Hospital on August 7, 1933. Six weeks previously he had been struck on the right brow by a cricket ball and developed a black eye, but remained well till one week before admission when he began

to have frontal headaches, followed two days later by vomiting, succeeded by drowsiness and anorexia. No history of nasal trouble at any time.

Examination.—Temperature 103° F. Pulse 110. Ill-looking boy, with very tender fluctuating swelling just to right of midline of forehead. Routine neurological examination negative save for very slight lower right facial weakness, diminished abdominal reflexes and a doubtful right extensor plantar response. Blood-count: 14,200 white cells, 80% polymorphs. *Diagnosis.* Acute infective osteomyelitis with superficial abscess. Extradural abscess. ? Left frontal abscess.

First operation (statim).—Evacuation of superficial abscess. Perforation and removal of small area of frontal bone. Evacuation and drainage of extradural abscess. Pus: *Staphylococcus aureus.* Brain not explored.

Subsequent progress.—His general condition improved, although he ran the high intermittent temperature of acute osteomyelitis. On the third day he complained of pain in left thigh; this subsequently proved to be due to a subacute metastatic focus in femur. He was carefully observed for the development of any signs indicating intracerebral involvement and these duly appeared. In a fortnight he developed a definite right extensor plantar reflex and slight lower right facial weakness. In the fifth week his pulse-rate was for two days in the 50's and he had three small vomits. His general condition was very good and no interference was made. In the eighth week the pulse again slowed, vomiting was more marked, headaches and drowsiness occurred, and a slight right-sided weakness appeared. No papillœdema. No aphasia. No mental symptoms. Lumbar puncture not performed.

Second operation (September 28, 1933).—Exploration of left frontal lobe through fresh burr hole to left of midline. Drainage of abscess one centimetre deep to cortex. Pus: *Staphylococcus aureus.*

Subsequent history.—Uneventful recovery. The abscess was drained for eight weeks. He was discharged on January 3, 1934, all neurological signs having cleared up and wounds having healed.

Cerebral Abscess (Right Frontal Lobe) following Traumatic Infective Osteomyelitis of Frontal Bone.—CHARLES DONALD, F.R.C.S.

F. K., male, aged 53.

History.—On September 7, 1932, he was hit on the forehead by a crowbar. He was dazed but not unconscious. The skin was broken and bled a little but healed up rapidly. Two weeks later he started to have frontal headaches; six weeks later a swelling occurred at the site of the accident and discharged pus spontaneously. Admitted to London Hospital on October 28. No abnormal neurological signs found. X-rays showed several small sequestra in a limited area of osteitis. On November 20 the wound was explored, six small sequestra removed and an extradural abscess drained. The dura itself was covered with rough granulations. By December 16 the discharge had practically ceased; he was free from headaches and he was discharged. His temperature had never been above 99° F.; his pulse had never been slowed.

On May 1, 1933, five months later, he was readmitted, having for four days been unsteady on his legs, apathetic, depressed even to crying, sick and complaining of headaches. His wife stated that during the previous few months he had been somewhat forgetful and had had occasional headaches, but, on the whole, had been very well.

Examination.—Temperature 98·4° F. Pulse 60. Drowsy, apathetic, disorientated and resentful of examination. The wound on the forehead had healed and there was no bulging over the bony defect. He had bilateral papillœdema of 1 D, slight left-sided paresis and an occasional extensor response in the left toe. *Diagnosis:* Left frontal lobe abscess. Lumbar puncture was not performed.

Operation (May 4, 1933).—Exploration and drainage of left frontal lobe abscess, through fresh opening just to right of midline. Thick green pus (*Staphylococcus aureus*) found 2 cm. deep to cortex.

Subsequent progress.—The general condition improved quickly but the mental condition remained impaired for some four weeks. He was apathetic, talked in monosyllables and then nonsensically. When asked if he knew where he was, he would say "Somewhere in the Tidal Basin." (He had been a dock labourer.) He had occasional incontinence. Quite quickly, however, within a few days of the end of this period he became quite rational, interested in his surroundings, and talked well.

The abscess was drained for seven weeks. After removal of the drain, the wound healed quickly. His abnormal neurological signs had completely disappeared by July 3, 1933, when he was discharged. He has remained perfectly well since.

Cerebral Cysticercosis with Epilepsy.—D. DENNY-BROWN, M.B.

P. T., male, aged 31, admitted to Guy's Hospital under Dr. Symonds November 3, 1931, on account of epilepsy and failing vision. No family history of epilepsy could be elicited. He had had poor vision in the left eye as long as he could remember. In 1924, while stationed in India, he contracted malaria. While convalescing he had an attack of unconsciousness, followed by prolonged amnesia. He is unable to give a clear history of this period. Sent back to England, and from that time suffered from fits at irregular intervals. Each attack was preceded by involuntary shaking of head, passing into generalized convulsion, and followed by severe headache. In 1927 and in July 1931, he had periods of frequent fits (? *status epilepticus*), with severe headache, but had only very hazy recollection of them. He had had one right-sided attack, affecting the right hand and arm, two months before admission. He was certain that vision in left eye had been progressively deteriorating since 1924. One week before admission he suffered from severe right-sided frontal headache, with blurred vision in the left eye.

On admission.—Pallor of both optic discs, more marked on the left side, with some blurring of the medial border of both discs. Both pupils slightly irregular. No other abnormal physical signs. Cerebrospinal fluid: Pressure, 225 mm.; residual pressure after withdrawal of 8 c.c., 215 mm. Cells nil; protein 0·05%, chlorides 740 mgm. %. Skiagram of skull revealed very numerous scattered points of calcification up to the size of a pin-head throughout the brain, both superficial and deep, but not below the tentorium. The limbs were X-rayed for other evidence of the disease but none was found. The discs became more blurred, and the patient was observed to have a persistent right extensor plantar response after some attacks. An encephalogram showed no definite distortion of the ventricles. In December 1931 Mr. Bromley made a right temporal decompression. No abnormality of the cerebral cortex could be detected at operation. Since that time he has continued to suffer from intermittent frontal headaches and from minor attacks preceded by shaking of the head and followed by confusion, amnesia, and headache. Occasional attacks of paræsthesia over the whole left side and, less frequently, similar attacks affecting the right upper limb. Regular luminal and bromides control the attacks to some degree, so that he loses consciousness only very infrequently. Vision poor in left eye, more obvious pallor in both discs, right more than left. No fresh abnormality of physical signs. Plantar responses both flexor. Further skiagrams of skull in January 1933 revealed no change in calcification.

The optic atrophy in this patient is particularly interesting. Mild optic neuritis with consequent atrophy has been described commonly in cerebral cysticercosis and due either to hydrocephalus or to basal meningitis. When he was first seen it was thought that here there was hydrocephalus. An encephalogram

showed that the ventricles filled readily. They were not definitely pathological, though they were slightly enlarged. The decompression does not bulge. There is no evidence therefore that the patient has chronic hydrocephalus. The surgeon could see no abnormality on the cortex. In published accounts of autopsies on such cases, though the cysts are in the pia, they are more common in the fissures, and that is perhaps the reason why nothing abnormal was noticed on the surface.

Discussion.—The PRESIDENT asked Dr. Denny-Brown what he regarded as the pathogenesis of the epilepsy seen in association with cerebral cysticercosis.

Dr. DENNY-BROWN (in reply) said the condition was, pathologically, accompanied by a good deal of meningeal fibrosis, and cortical gliosis; he thought one might reasonably blame the gliosis for the epilepsy.

Cysticercosis.—S. BEHRMAN, M.R.C.P.

Patient is an ex-soldier who served in India from 1926 until 1929. Tapeworm infection occurred in 1927 and segments were last seen in December, 1929, but he never received any anthelminthic treatment.

Dr. Behrman's case of cysticercosis.

In June 1928, he had the first fit which began with severe convulsive movements of the abdominal muscles, and this was followed by movements of the right arm before loss of consciousness. During December 1928, he had six major fits within a period of forty-eight hours. During spring 1931, he had the third major fit.

Since then he has been subject to sensory and local motor fits. The following sensory fits usually occur without any motor disturbances: "Feeling like electricity in the right thumb"; "burning pain in left thumb and forefinger"; "numbness in left big toe"; "flashes of orange light" in left visual field. Local convulsions have

always been confined to the right side of body and have occurred in the hand, face and legs, and have been frequently associated with temporary loss of speech.

Two other soldiers in the same regiment contracted tape-worm infection, and subsequently had epileptic seizures.

On examination no superficial cysts can be palpated.

Central nervous system: No abdominal physical signs.

Skiagrams: Numerous calcified cysts can be seen in skull and muscles.

Discussion.—Dr. MACDONALD CRITCHLEY said that for some time he had been interested in this condition, and last year, through the kindness of Colonel MacArthur, he saw a number of instances of it at the Millbank Medical College. This disorder was now being recognized as a common cause of epilepsy in a certain type of person in this country, and in March last Colonel MacArthur collected 22 cases; by last December the number totalled 60. The subjects were young adults, without any family history of epilepsy; they had all been soldiers and had served in India, and in almost all of them the first attack came after they had arrived at their 21st year. In very few of the cases was there to be derived a positive history of infection with tinea.

The diagnosis was made by one of four criteria: palpation of subcutaneous nodules of calcified cysts; skiagraphic demonstration of them in the muscles or in the skull; the presence of eosinophils in the spinal fluid, not a common finding; and fourthly, a positive complement-fixation test.

The PRESIDENT said that there must have been hundreds of thousands of soldiers in India long before the last few years, and he wondered whether this condition had only recently been recognized, or whether there was some brand of cysticercosis which had only made itself evident of late.

Dr. MACDONALD CRITCHLEY said that cysticercosis had long been known as a cause of epilepsy, but recently the Millbank authorities had been sending for soldiers who were invalided out of the Army because of epilepsy, and were finding that a large proportion of them had cysticercosis.

Dr. RUSSELL BRAIN said that one feature about these two cases was the variability in the character of the attacks, and he asked whether that feature had any diagnostic value. These patients had attacks of focal onset, but shifting as to site from time to time. On one occasion an attack would begin in the right hand, then one would start in the left hand, and one had tonic fits. At another time an attack began with spasm of the left hand, and his last patient had focal attacks, suggesting a focal lesion in one leg area, beginning on the same side, then, after a few months, an attack began in the opposite leg. That behaviour was to be expected because of the multiple lesions.

Nystagmus (Rhythmical Myoclonus) of the Palate and Tongue.—Shown by D. DENNY-BROWN, M.B.

W. W., male, aged 46. First attended Department for Nervous Diseases, Guy's Hospital, in December 1929, complaining of slurring of speech, weakness of right arm and leg, and giddiness, of sudden onset and fourteen days duration. He had had a primary chancre in 1919 with full course of treatment. No history of any other illness.

On examination.—Slurred dysarthria; right pupil reacted sluggishly to light. No nystagmus, no strabismus. Weakness of right side of face, no weakness of palate or tongue, and no tremor. Some loss of tone, with cerebellar inco-ordination in the right arm and leg, both plantar responses extensor. Right ankle-jerk brisker than left. No sensory loss. Blood Wassermann reaction ±. Ætiology has remained uncertain.

He was given a course of novarsenobillon and prolonged treatment with iodides and mercury. In June 1931, August 1932, and April 1933 the blood Wassermann and Kahn reactions were negative.

Speech still remains slurred, with scanning when patient is nervous. Face stiff and spastic. Slight rotatory nystagmus of eyes on looking to left, very fine rotatory nystagmus of both eyes at rest. Pupils react well to light and to accommodation. Face stiff and spastic. Slight action tremor of right upper limb, and slight regular tremor when outstretched. Tendon-jerks very brisk, both plantar responses extensor, with indefinite spasticity of both lower limbs.

The palate, and to a less degree the tongue, show a regular tremor at rest, of similar frequency to that in eyes and right hand. No tremor of head or of lips.

The pathological diagnosis is not clear. He apparently has multiple lesions because though there is evidence of a right-sided pontine lesion, both plantar responses are extensor.

Discussion.—Dr. DENNY-BROWN: In view of your work, Mr. President, I would like to ask your views on the pathology of the facio-respiratory movements—whether you think they might come into the category of this movement in this case—badly called nystagmus, which means a nodding—and, in particular, I ask whether, as Freeman suggested recently, this might be a continual mild yawning movement, freed by some lesion in the brain stem.

The PRESIDENT (replying to Dr. Denny-Brown) said it was, he thought, an escape movement, and it must be ponto-medullary, or cerebello-ponto-medullary. One could get palatal "nystagmus" (a term he agreed in criticizing) from lesions of the cerebellum anywhere below that level, but above the level of the foramen magnum. He did not think the movement in Dr. Denny-Brown's case was very rhythmical; it was nearly always irregular. He had always looked upon it as a tremor, a movement which might be caused by a lesion of one or other side. It was impossible to dissociate the two voluntary movements of the palate. He had thought it was due to interference with the rubro-pontine or rubro-bulbar nuclei. It must be the nucleus ambiguus which was set free, and it was necessary to postulate some lesion which was above that and was permitting it to occur. The question was, Where above it? It must be somewhere above both nuclei, because one nucleus was affecting one side, and, he thought, one side only. That left the possible area a wide one.

The case presented several unusual features; for example, the rotatory character of the nystagmus, which was characteristic of syringobulbia as compared with other forms of nystagmus. These lesions were low in the pons or high in the medulla. He did not know whether the Wassermann reaction was a "blind," and whether the man had another condition.

Amyotrophic Lateral Sclerosis of Unusual Distribution.—E. A. BLAKE PRITCHARD, M.D.

Patient, a woman, aged 65, with shortening of the left leg due to old osteomyelitis. Now showing spastic paraplegia with wasting of muscles of the right leg and intrinsic muscles of both hands.

History on admission, September 26, 1933:—

One year ago.—Some septic inflammation of right foot which prevented her from working for three months.

Nine months ago.—First noticed weakness of right foot, being unable to lift it up on to the kerb. Recurrence of inflammation in the foot.

Six months ago.—Attended Royal National Orthopædic Hospital complaining of numbness and coldness of right leg, which was blue and the ankle swollen. Was there considered to be suffering from osteoarthritis of right hip. During the past six months the leg has been getting thinner. Two months ago she began to complain of pain in the back and of pain radiating up the right leg, which has since increased in severity. During the same period the right leg became progressively weaker and very stiff, so that for the past two weeks she has been unable to walk on the leg.

Past history.—Operation at age of 7 years for osteomyelitis of the left femur with septic knee-joints.

On examination.—An intelligent woman. No cachexia. The left leg is 4½ in. shorter than the right, with arthrodesis of the left knee-joint and a marked compensatory scoliosis. The right leg cannot take the patient's weight.

Central nervous system: Apart from irregularity of right pupil and slight ptosis of left lid, no abnormality of the cranial nerves.

Arms: Some weakness of grasps and slight wasting of intrinsic muscles of hands, with exaggerated reflexes, but no inco-ordination.

Abdomen: Superficial reflexes are present and equal.

Legs: Knee fixed. Weakness of dorsiflexion of ankle; the toe movements poor. Hamstring and adductor jerks exaggerated; ankle-jerks brisk.

Right leg: Wasting of vastus internus and calf muscles, with extreme weakness of ankle and toe movements. Abduction and adduction of hips, fairly good. Knee-jerk exaggerated; hamstring and adductor jerks brisk; ankle-jerks absent. Plantar response absent, but there is brisk flexion of knee.

Sensory system: Apart from slight impairment of vibration-sense over both legs, more marked on right than left, no loss of cutaneous or deep sensibility.

Cardiovascular system: Heart normal. Blood-pressure 145/85.

Chest: Right basal fibrosis with a scar of thoracotomy for empyema following pneumonia in 1925.

Abdomen: Normal. Blood Wassermann reaction, negative.

Cerebrospinal fluid: Normal pressure. No block; no increase in cells or protein. Wassermann reaction and Lange, negative.

Blood-count: Normal.

Skiagrams: Osteoarthritis of both shoulders, right hip, right knee and lumbar spine, right side only. Marked scoliosis.

Electrical reactions: Left leg normal.

Right leg: Quadriceps, normal; hamstrings, normal; extensor digitorum, diminished faradic response; tibialis anticus, diminished faradic response; extensor hallucis, no faradic response, galvanic response normal; flexor digitorum and other calf muscles, normal.

Progress.—Pain in the back improved on application of radiant heat to the spine. There has been slight increase of power in the right leg following massage and exercises. The other signs are as on admission.

Dr. RUSSELL BRAIN said that some significance must be attached, in this case, to the infection of the foot, which preceded the symptoms in the right leg by only three months. He saw this patient a little time ago, and thought he probably had an ascending infection involving the lumbo-sacral plexus on the right side, due to the original focus in the foot.

Post-traumatic Optic Atrophy.—E. A. BLAKE PRITCHARD, M.D.

J. M., a girl, aged 12, was normal in every way until Easter 1932, when she fell while playing at school and struck the back of her head. She did not lose consciousness but vomited immediately afterwards. Twenty-four hours afterwards she appeared to have recovered completely. *Three months later* she suddenly complained of pain over both eyes and failing vision in left. Examined at Western Ophthalmic Hospital, where her visual acuity was found to be R. $\frac{6}{5}$, L. $\frac{6}{60}$. Right disc was normal; left, pale. Pain over the eyes did not last for more than a week. *Nine months later* she noticed that vision with the right eye was impaired. Examined again at same hospital and found to have visual acuity of $\frac{4}{60}$ in right eye and $\frac{5}{60}$ in left eye, with pallor of both discs and bilateral central scotoma. On three occasions during the past four months she has fallen, with sudden loss of consciousness: she was paler than usual but had no convulsions or incontinence of urine. After each fainting attack she vomited.

On examination.—She is seen to be pale, although her blood-count is normal in respect of erythrocytes and hæmoglobin. Pupils dilated and fixed to light and on attempted convergence. Both discs small and white. Retinæ otherwise normal. Visual acuity does not extend to counting of fingers held in front of either eye. Visual fields full at periphery. There is an absolute central scotoma extending 3° around the fixation point in the right eye and 10° in the left eye. Neurological examination is otherwise negative in all respects.

Skiagram of skull normal. Wassermann reaction negative in blood and cerebrospinal fluid. The cerebrospinal fluid is normal in respect of all usual tests. The accessory nasal sinuses were examined and reported normal.

She has one sister, aged 5 years, who is normal.

It is a question whether this condition is related to the accident, or whether it is a form of Leber's retrobulbar neuritis followed by atrophy. There is no family history.

? Delayed Cortical Cerebellar Atrophy. ? Familial Tremor.—E. A. BLAKE PRITCHARD, M.D.

H. A., aged 59, a house painter, was first seen in February 1932, when he complained of shaking of his left arm only when this was in use. He had had pains in the abdomen and some trouble with his teeth; these were extracted four years previously, and he was told that the trouble was due to lead poisoning. When examined no physical abnormalities were found, beyond an unhealthily pale complexion, marked arcus senilis and shaking of the left arm when it was held extended in front of him, with exaggeration of this tremor towards the end of precisely directed movements.

He has attended the out-patient department regularly since. During this period of two years the inco-ordination of movement has increased in the left arm and has appeared and progressed in the right arm also. Within the past six months some titubation of the head and unsteadiness of the trunk have been noticed. The general health has, on the whole, improved, and there is more colour in the face. He finds drinking from a cup now very difficult because of the shaking of his arms, and two minor accidents have resulted from his unsteadiness; once he jerked a kettle of boiling water off the stove, scalding his leg, and on another occasion he fell off a 'bus into the road; he was holding the hand-rail and felt himself jerked off by a pull of his arm. He has bilateral deafness which is not progressive and which appeared suddenly while he was working in a munition factory during the late war.

On examination he now shows the above symptoms of arcus senilis, intention tremor of both arms, with no unsteadiness while they are resting, and titubation. Pupils small, but otherwise normal in every respect. Fundi normal. The visual acuity is $\frac{6}{6}$ in each eye; fields are full. No nystagmus.

No weakness or wasting of limbs. Tendon reflexes and superficial reflexes normal. No inco-ordination of movements of legs. Blood-pressure 145/80. Blood-count normal; no punctate basophilia.

His mother's eldest brother, an upholsterer, became, at the age of 60, so shaky in his movements that he could not write or pick up any small object such as his tacks. The patient worked for him and helped him in these ways until the uncle was forced, because of increased shakiness, to give up work. He died at the age of 68. His two brothers were not similarly affected.

Discussion.—Dr. BLAKE PRITCHARD: I think this is an example of what the President has mentioned—a case not falling completely into any recognized group. The usual bilateral intention tremor in the arm appeared in this patient at the age of 59, and has not yet spread to any other part of his body. An uncle suffered at the same age from the same symptoms. It is later than is commonly accepted for the onset of familial tremor, and at the age at which inco-ordination and cerebellar atrophy is held to appear, but with a familial incidence.

Dr. MACDONALD CRITCHLEY said he doubted whether these two diagnoses were mutually exclusive, because, for a long time, he had thought that the two conditions were very intimately associated. He had been watching cases of familial tremor, and had collected records of many such families. The tremor might appear at any age ; it could start at 80, or during the first few months of life. Some of these cases developed other signs in the nervous system which were of the cerebellar order, so that as time progressed the case came to resemble a senile or pre-senile cerebellar atrophy. One case had been recorded by Professor Schuster, of a family in Berlin with familial essential tremor, some members of which later developed olivo-pontine cerebellar atrophy.

Pituitary Basophilism.—E. A. BLAKE PRITCHARD, M.D.

F. B., a single woman, aged 41, developed normally and was free from symptoms until the age of 26 or 27, when she then began to complain of malaise, polyuria, increase in weight and increasing redness of face. This was in 1920.

In 1924 she was admitted to University College Hospital for the first time. She was then obese, there was excessive hair growth over the face, she had some tremor of the hands, prominence of the eyes and tachycardia (90 per minute). Her blood-pressure was then 140 mm. Menses regular since the age of 13. Urinary output not increased. Blood-count normal. Blood-sugar 0·114%.

In 1925 she began to complain of attacks of sudden transitory loss of consciousness in which she fell but showed no other abnormal symptoms beyond pallor. Her condition on examination was the same as in 1924.

In 1926 she began to complain of aching pains in the legs and of a pain in the right loin.

In 1927 the hairiness of her shoulders and chest was found to be increasing.

In 1928 (May) the attacks of loss of consciousness became more frequent and exophthalmos more obvious. The hair on the scalp was obviously thinning while that on her face was increasing.

In 1928 (October) she was examined by the hospital psychiatrist because of recent violent outbursts of temper. He considered her to be mentally normal and psychically feminine in temperament.

In 1931 she began to complain of increasing pains in the legs. The radial arteries were found to be hardened and thickened and the blood-pressure had risen to 190.

In 1932 she again complained of polyuria and while in the hospital had an attack during the night in which she was unconscious and convulsed. She was then given deep X-ray treatment to the head.

In 1933 (April) she had, while at home, an attack of unconsciousness with generalized convulsions, cyanosis and incontinence of urine. She had had no menses since the X-ray treatment and the polyuria had diminished.

In 1933 (November) she was readmitted for further X-ray treatment and her condition on examination has remained unaltered up to the present.

Present condition. — Slightly over weight : fat distribution maximal over shoulders and chest ; excessive redness of face and chest with pigmentation of eyelids and of breast areolæ ; excessive hairiness of face, shoulders, arms and chest ; the suprapubic hairs extend up to the umbilicus. She shaves her face daily and wears a wig which covers short, scanty, fine hair ; of average intelligence and normal emotional control. Her visual acuity right and left is $\frac{6}{6}$; the visual fields full to 0·5° white ; colour fields normal to 15/2000 red. Fundi and discs normal ; eyes somewhat prominent ; no impairment of cranial nerves ; no weakness or incoordination of movements of limbs and no abnormality of superficial or deep reflexes. No impairment of cutaneous or of deep sensibility.

Cardiovascular system.—The blood-pressure readings have been as follows :—

1926	132/148 mm. Hg	1931 (Nov.)	180/210 mm. Hg
1928 (Jan.)	140/172 „ „	1932 (Nov.)	170/210 „ „
1928 (Oct.)	150/220 „ „		

Heart slightly enlarged. Pulse-rate averages 90. Palpable arteries unduly thickened.

Skiagrams.—Legs : Calcification of femoral and tibial arteries and of their branches.

Skull : no enlargement of pituitary fossa and no other changes in bones.

Spine : no abnormalities of vertebræ.

Blood-count.—R.B.C. 5,600,000 ; Hb. 106% ; C.I. 0·96 ; W.B.C. 8,200. *Differential* : Polys. 80% ; lymphos. 17% ; mononuclears 1% ; eosinos. 2%.

Blood-sugar : Resting, 0·114%. Blood-sugar curve shows a delayed fall. Blood-urea, 51 mgm. %.

Urinary output at present varies between 75 and 116 oz. daily (average 90 oz.) No abnormalities on microscopic or chemical examination.

Urea concentration test gave normal results.

Blood cholesterol : 145 mgm. per 100 c.c.

Blood metabolic rate (1926) : + 50%.

Exploratory laparotomy (1928, because of persistent pain in the right loin), showed no abnormality of the right suprarenal body, no enlargement of the kidney and normal pelvic organs, by palpation.

Skiagrams.—Long bones show general rarefaction of bones.

Discussion.—Dr. BLAKE PRITCHARD : She has been an in-patient at University College Hospital on many occasions during the last five years and was originally labelled "polyglandular syndrome." On Professor Harvey Cushing's visit to this country the diagnosis was changed to pituitary basophilism. Yet I think the earlier diagnosis may fit the case better. A case which shows so many symptoms is not necessarily pituitary in causation.

Dr. E. STOLKIND said he was particularly interested in this case, as he had under his care a similar one, that of a plethoric, round-shouldered woman aged 25, who, ten years ago, noticed that hair began to grow over her face. She now had a beard and moustache and had to shave ; the pubic hair extended up the abdomen, and there was hair on the chest, as well as on the extremities. She had a blood-pressure of 230 to 250, purplish lineæ atrophicæ, adiposity, albuminuria and a few casts in the urine, polycythæmia, headaches, etc. His view was that she had in all probability, besides pituitary basophilism (Cushing), an affected adrenal cortex. In his opinion the adrenals might be also involved in the case shown by Dr. Pritchard.

Dr. F. PARKES WEBER said there seemed no doubt about the existence from the clinical point of view of the group of cases which were described by Harvey Cushing, though the clinical syndrome included a great variety of symptoms, some of which were absent or not prominent in some cases. The present patient had shown no evidence of severe kidney disease, and there were no eclamptic or uræmic attacks, and there was no glycosuria. Probably some of the "bearded women with glycosuria" belonged to the same group. Much pathological [anatomical and histological] evidence had been brought to show that all these cases might be results of the presence of minute basophilic adenomata in the anterior part of the pituitary body ; for the moment one might neglect the idea of a mere increase of the basophilic cells in question. A point on which fresh evidence was required was, how often a minute basophilic adenoma of the pituitary gland was present at all autopsies on all kinds of cases. Work was now being done at certain pathological institutes to settle that point ; it could only be done by cutting serial sections of every pituitary gland, so that not even a very minute adenoma could escape detection. Until that point had been decided he thought Harvey Cushing's suggestion should not be accepted in its entirety.

One suggestion was that whenever there was over-action of glandular cells, there existed a tendency to the formation of adenomata, or even adeno-carcinomata. One might suppose that there was a reciprocal action between the basophilic cells in the pituitary gland and the

glandular cells of the suprarenal cortex, so that when the latter were much too active, an excessive functional activity of the basophilic cells in the anterior part of the pituitary gland was secondarily likely to be present also; and it would not be surprising that under such circumstances minute basophilic adenomata of the pituitary gland should occasionally develop. By way of analogy it might be remembered that in cases of fibrosis of the liver or kidneys, when there was excessive work thrown on the surviving cells of these glands, it was not very rare to find evidence of compensatory cellular hypertrophy or hyperplasia accompanied by actual neoplastic formation (minute subcapsular papillary adenomata in the kidney, or adenomata or even adenocarcinomata in the liver).

The PRESIDENT said he ranged himself with those who felt that Harvey Cushing's thesis still remained unproven. The most interesting feature in this case was its suprarenal aspect; it reminded him of Dr. Turney's case, which he saw at the Royal Society of Medicine[1] before this syndrome was heard of. Turney's article was supported by striking photographs, showing the lady in a charming gown, and another depicting her a year or two afterwards when she was completely metamorphosed like the lady seen this evening. He remembered the description of a French case in which the woman was named "The Tiger," because she had changed so much in her character as a result of this disease. The violent outbursts of temper in these cases were probably not due to the femininity of the patient, but to the conflict between her normal self and the virility which came into force in some pathological states of this kind. This was a syndrome, or one might call it a mosaic, and the prime cause might be suprarenal, though it might occur in a wider syndrome.

Epilepsy, and Parathyroid Disturbance with Cataract.—E. A. BLAKE PRITCHARD, M.D.

D. K., a boy, aged 13, was first seen in February 1931, at the age of 10. He was an only child, preceded by a five months' miscarriage and delivered at term by Cæsarean section. At the age of 5 he fell and hit his forehead against a brick wall; he did not lose consciousness and no sequelæ beyond a large bruise were noticed. Four months later he began to have fits which have continued ever since. He occasionally complains of feeling bad for a few seconds before each fit but usually he falls without warning, becomes stiff and cyanosed and then twitches in all his limbs. He has bitten his tongue and passed urine on several occasions. Loss of consciousness lasts for a minute or two in some of these attacks but usually for only a few seconds.

After receiving treatment at Great Ormond Street Hospital he was free from attacks for one year. Then, at the age of 6, he had whooping-cough and discontinued treatment; the fits began again and have never entirely disappeared. The longest interval, during 1930, i.e. at the age of 10, was one month, and at the end of that year the fits were of daily occurrence.

From the age of 7 to the age of 10 he has had, also, attacks of partial consciousness with stertorous breathing. He was said to be well in every way, not to complain of headaches, to eat perhaps too heartily, and to be quite active on his legs.

On examination, March 1931, he was backward for his age, 10 years, being unable to read. Cranial circumference large but within normal limits. Visual acuity apparently normal. Retinal veins rather thick but no other abnormality of fundus. Pupils normal in size and reaction. No impairment of function of cranial nerves. Light percussion over parotid region on either side resulted in a twitch of all the facial muscles of the same side. No impairment of power or of co-ordination of limbs; gait rapid and normal. Sphincter control perfectly good; no impairment of any form of cutaneous sensibility. Tendon reflexes were all brisk and equal, and plantar responses flexor. Compression of the upper arm with sphygmomanometer band at 180 mm. Hg pressure for five minutes resulted in no spasms of the hands.

[1] *Proceedings*, 1913, vi, Sects. Neur. and Ophth. (combined meeting), lxx.

Between March 13 and 20, while in hospital, he had up to twenty minor epileptic attacks daily; during this period he was not receiving medicine. On March 19 he was put on to ½ gr. of luminal twice daily and 20 gr. of calcium lactate, and no further epileptic attacks were observed during his stay in hospital for a further six weeks. He had one attack of stridor and cyanosis with loss of consciousness but no convulsions, on March 30. For six hours he remained unresponsive to questioning or stimulation, with rapid (30/min.) breathing with much inspiratory stridor: expiration was noiseless. His temperature rose slightly but his pulse-rate was unaffected. Examination of larynx showed no abnormality. Skiagram of skull showed normal sella turcica; skiagram of chest showed no evidence of thymic enlargement. Blood Wassermann reaction, negative.

He left hospital on April 30 and has attended the out-patient department since. He remained free from epileptic attacks until January 1933, and was receiving during this period ½ gr. of luminal twice daily. In January 1932, he had several attacks of laryngismus and calcium lactate was added to the luminal. He was free from both varieties of attack until June, when another attack of laryngismus occurred and in August one slight minor epileptic attack was noticed.

In September 1932, he began to complain of headaches. He was examined again by the ophthalmic surgeon because a left internal strabismus had developed. His visual acuity at that time was recorded as $\frac{6}{6}\bar{0}$ in each eye and an opacity of both lenses was noted.

In January 1933, he had a return of several minor epileptic attacks. His mother said that he had increased greatly in weight, and weighing at each Out-patient attendance showed an increase from 5 st. 3 lb. in January 1933, to 5 st. 8 lb. in October 1933.

No further epileptic attacks or attacks of laryngismus have occurred. His eyesight has steadily deteriorated and he now has difficulty in getting about anywhere except at home. He does not complain of headache and seems well in every other respect.

The accident at an early age may have had some influence on the development of the epilepsy. The problem now is as to whether needling of his cataract is likely to result in permanent improvement of sight, or whether this operation will do anything more than temporarily relieve the opacity of his media.

Dr. PRITCHARD (in reply to a question) stated that the patient was given calcium for several weeks but luminal was given at the same time, and there was no reduction in the frequency of the attacks attributable to the calcium.

Section of Physical Medicine

President—M. B. Ray, D.S.O., M.D.

[*January* 19, 1934]

DISCUSSION ON THE TREATMENT OF MUCOUS COLITIS.

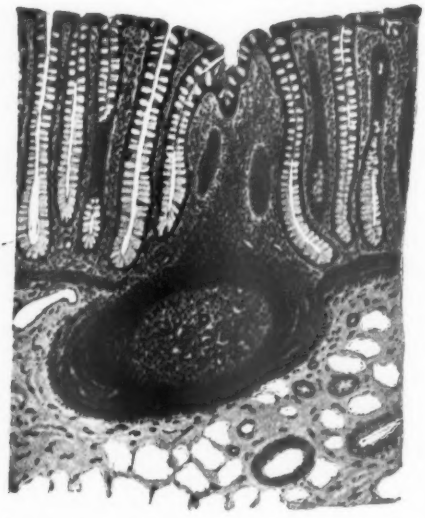
Dr. Arthur F. Hurst: Specialism in therapeutics has dangers which are even greater than those of specialism in other branches of medicine. It is natural that an expert in any special line of treatment should sometimes be tempted to accept without question the diagnosis already made in patients sent to him and to apply treatment without sufficiently full consideration of the nature of their complaints. Thus, a patient diagnosed as suffering from mucous colitis, may be treated by vaccines if sent to a bacteriologist, by Plombières douches if sent to a spa, and by diathermy if sent to an electrotherapeutist, although a fuller investigation might show that the so-called mucous colitis was a result of achlorhydria and could be rapidly cured by means of gastric lavage or the administration of hydrochloric acid, or that it was the first manifestation of a carcinoma of the pelvic colon, which might pass from a stage in which successful surgery was still possible to one of inoperability, whilst some useless form of treatment was being carried out. These instances are not imaginary. I have seen many private patients who have for weeks or months had treatment of the kinds I have mentioned for so-called mucous colitis, when subsequent investigations have shown that they were really suffering from achlorhydric gastritis or carcinoma of the colon.

When I was invited to open this discussion, I was at first inclined to reply: "There is no such thing as mucous colitis, so I cannot open a discussion on its treatment." On reconsideration, however, it occurred to me that I might instead attempt to explain why I object to the diagnosis of mucous colitis and at the same time point out what disorders of the colon seem most suitable for physiotherapy.

Strictly speaking, mucous colitis means inflammation of the colon associated with the passage of excess of mucus. It is therefore necessary to consider under what conditions excess of mucus is passed. The secretion of mucus is a function of all mucous membranes. A section of the normal mucous membrane of the human colon shows that a large proportion of cells of the lining epithelium, including that of the crypts of Lieberkühn, are goblet-cells (see fig.), the function of which is to protect the mucous membrane from injury by the secretion of mucus. Mucus is in fact the only important product of the secretory activity of the colonic mucous membrane. The secretion is increased in response to mechanical and chemical irritants. Hard fæces in the pelvic colon and rectum act as mechanical

irritants. Consequently the dry scybala passed in dyschezia—the very common pelvi-rectal form of constipation—are covered with mucus, which contains no inflammatory products, such as leucocytes or red corpuscles, and no bacteria beyond a small number of the *B. coli communis* and enterococci which inhabit the healthy colon. Endoscopy in such cases always reveals a perfectly healthy mucous membrane. It is clear, therefore, that excess of mucus with hard scybala should not lead to a diagnosis of mucous colitis.

The most common chemical irritants of the colon are purgatives. As they lead to purgation by irritating the colonic mucous membrane, they naturally also call forth an excessive secretion of mucus, which contains no leucocytes or red corpuscles, and endoscopy again shows no abnormality in the appearance of the mucous membrane. The mucus indeed protects the mucous membrane so efficiently that



Mucous membrane of the human colon, showing numerous goblet cells in the crypts of Lieberkühn. × 70. (After Braus.)

actual colitis only results when very large doses of purgatives have been taken for very long periods. In such cases the diarrhœa induced by the purgatives persists when their use is discontinued. It is clear, therefore, that excess of mucus with soft or liquid fæces in a patient taking aperients does not justify a diagnosis of mucous colitis.

Another common cause of chemical irritation of the colonic mucous membrane is the use of irritating suppositories, enemas and douches. Glycerine suppositories and enemas, though useful under exceptional conditions, always call forth an abundant secretion of mucus, unaccompanied, however, by any evidence of proctitis. Soap enemas and all kinds of medicated enemas and douches give rise to similar, but often less intense, irritation. Most natural waters used for douching at spas have also a slightly irritating action, though, if isotonic, this may be negligible.

Normal saline solution is almost the only fluid which does not as a rule stimulate the secretion of mucus. Patients frequently bring illuminating reports from the people in charge of colon laundries, the excellent American name for the institutions, of which there are far too many in London, where intestinal lavage is practised. The following is typical: The patient was a boy of 18, who had always had a tendency to constipation and had been continually dosed by his mother with aperients. His report stated that he had been given an irrigation of thirty pints, the treatment lasting one hour and ten minutes.

"The first twelve pints brought away loose fæces but no mucus, but after that a large quantity of jelly mucus was passed continuously until the end of the treatment."

That is to say, twelve pints of fluid were required to irritate the healthy mucous membrane of this boy sufficiently to produce excess of mucus, but when once it began to be secreted it naturally continued, and there would still have been mucus present if he had received a hundred instead of only thirty pints. I have often seen patients diagnosed as suffering from mucous colitis, although they had never passed mucus until Plombières douches had brought some away; it was sometimes reported that by the end of the patient's cure little or no mucus was present, the true explanation being that the patient's mucous membrane responded at first by the secretion of mucus to the unaccustomed irritation, but after some weeks the mucus-secreting cells became exhausted and went on strike.

Lastly, when excess of undigested food reaches the colon, as in achlorhydric gastritis, and in enteritis, the colonic mucous membrane may respond to the irritation by secreting excess of mucus, although no colitis is present; achlorhydric gastritis is in fact the most common of all causes of chronic diarrhœa, the loose stools often containing excess of mucus.

It is clear, therefore, that mucous colitis can only be justifiably diagnosed if the mucus is passed with soft or liquid stools by a patient who is not taking aperients and who has not achlorhydria or enteritis. We must further exclude cases in which blood or pus is passed, as well as mucus, as, unless carcinoma of the pelvic colon or rectum is present, ulcerative colitis, or at least hæmorrhagic colitis, will be found on endoscopy. We are left with very exceptional cases of true mucous colitis, in which the patient passes liquid stools mixed with excess of mucus, containing excess of leucocytes and sometimes a few red corpuscles, and in which the sigmoidoscope shows that inflammation is present, though not sufficiently severe to be regarded as an early stage or a mild form of ulcerative colitis.

There is one condition which I have not yet mentioned—so-called muco-membranous colitis, in which the patient passes thin shreds or membranes, which sometimes form complete casts of a segment of colon several inches long. It occurs mainly in neurotic and and constipated women, but it is a remarkable fact that whereas up to 1914 it was quite common among private patients, it has become exceedingly rare since the war not only in England, but also on the Continent (Boas). This is in spite of the fact that uncomplicated colon spasm, with which it is always associated, is as common as ever. The disappearance of the condition is as mysterious as that of chlorosis. Many years ago Dr. Gordon Goodhart examined several such membranes for me; they were formed of coagulated mucus and contained no inflammatory material, and the sigmoidoscope showed a perfectly healthy mucous membrane. The condition, which is most appropriately known as muco-membranous colic (not colitis), as first suggested by Ewald, has many features in common with asthma. It depends upon abnormal irritability of the sympathetic nerve supply of the colon, and it is occasionally allergic in origin, the mucous casts representing the Curschmann's spirals expectorated by asthmatics, cases of pure colon spasm corresponding with the not uncommon cases of asthma, in which the secretion of mucus is very scanty.

Having done my best to demolish mucous colitis as a clinical entity, I must try to indicate what may usefully be discussed this evening. There are many men and women with uncomfortable colons, colons which are organically normal but functionally inefficient, who are very difficult to treat by diet and drugs alone. Their condition is often the result of abuse of aperients, occasionally the abuse of enemas, and a similar irritable colon is a very common sequel of intestinal infections, especially those contracted in the tropics, and may persist for years after the specific dysenteric or other organism has disappeared from the bowel. Muco-membranous colic and the various forms of colon spasm, which are not secondary to some organic disease such as ulcerative colitis or diverticulitis, may be included in this group. All such cases are suitable for physiotherapy, and I hope we shall hear of various methods of dealing with these difficult cases.

It is perhaps necessary to add that auto-intoxication resulting from stasis in the colon, which is the alleged indication for a great deal of treatment of different kinds, is a myth. Untreated constipation may cause local discomfort and is often a source of much anxiety to the patient, but it is very rarely the cause of toxæmia, as hard dry fæces do not undergo bacterial decomposition and, even if they did, it would be impossible for the mucous membrane to absorb anything from them. It is only when incompletely digested food is driven by purgatives from the small intestine into the colon, there to undergo putrefaction and fermentation, that intestinal toxæmia results. Apart from the abuse of aperients the absorption of excess of bacterial toxins or of toxins produced by excessive fermentation and putrefaction is not uncommon in the small intestine, especially as a result of achlorhydria, but it is rare in the colon except in specific infections such as bacillary dysentery. There is, for example, not a scrap of evidence that any form of arthritis is due, even in part, to auto-intoxication from the colon.

Lastly I should like to refer to one form of physiotherapy, which I have myself found of the utmost value in the treatment of the frequent functional disorders of the intestine which result from abnormalities of the anal canal. These include a congenitally small canal, a condition to which Lord Dawson drew attention twenty years ago, as a cause of constipation, and which I believe is by no means uncommon; acquired stricture following operations on hæmorrhoids; anusitis, with or without hæmorrhoids, and anal ulcer; and achalasia of the anal sphincter, which I believe is the cause of Hirschsprung's disease and megacolon. All these conditions can be relieved and often cured completely by diathermy, applied by means of a straight electrode—when no obstruction is present—and a conical one when there is spasmodic or organic obstruction or achalasia. Such treatment is infinitely preferable to cutting operations for such conditions as anal ulcer, and it is surely better to relieve the symptoms of megacolon by simple physiotherapy than by surgical interference with the nerve supply of the pelvic colon and rectum, an experimental form of treatment which is, at best, no more successful and which is occasionally followed by disastrous results.

REFERENCES

1 Boas, *Arch. f. Verdauungskr.*, 1933, liii, 416.
2 Lord Dawson, *Proc. Roy. Soc. Med.*, 1913, vi, Suppl., 249.

Dr. Geoffrey Holmes: As a spa practitioner, I see few cases of mucous colitis in their early stages. I have on several occasions seen cases of mucous colitis improve wonderfully after a bismuth meal or barium enema given for X-ray purposes.

It does not appear to be generally known that bismuth salts when given with a sufficient quantity of bromide do not cause constipation. I have found ten grains each of bismuth salicylate and bismuth subnitrate, suspended in a mixture with

fifteen grains of potassium bromide and a little sal volatile, taken three times daily before meals most effective in relieving gastritis and colitis accompanied by general abdominal tenderness and spasm of the colon.

The comparatively few cases of early mucous colitis which have come under my care have all cleared up satisfactorily with rest, warmth, a bland diet and prescriptions similar to the above.

In the more chronic cases I find that the patients usually tolerate a diet containing a fair amount of roughage and that both the general health and the condition of the colon improve more quickly on an all-round diet than on a milk and farinaceous diet, which has not infrequently been adhered to until the patient has become anæmic.

Of mucous colitis in its more chronic forms we see many cases in Harrogate. In some of these the mucous colitis is the main symptom, but it is often associated with other gastro-intestinal disorders, and is not infrequently found in cases sent up for treatment for rheumatism and arthritis.

The drugs I have found most useful are bromides, belladonna, hyoscyamus and codeia as sedatives and antispasmodics, and kaolin and salicylates for their detoxicating properties.

I have often noticed that when rheumatic patients are put on a mixture of sodium salicylate and sodium bicarbonate, gr. xv of each three or four times daily, stools which have been dark and offensive become pale and much less malodorous. Whether this is due to any action on the gall-bladder or the intestinal flora, or whether the action on the bowel contents in part explains the relief of the rheumatic conditions, I cannot say, but I have often seen salicylates bring about this improvement in the stools and the rheumatic conditions simultaneously.

In Harrogate whilst, as in other places, diet and drugs are used in the treatment of mucous colitis, the great majority of the cases are treated with the spa waters.

Abdominal packs are also used, but of these I need only say that any pack—whether the simple hot wet towel pack, the linseed poultice, the mustard poultice or the mud pack—is a helpful remedy for the relief of abdominal pain and spasm.

Mucous colitis is more often than not associated with disordered functioning of other parts of the gastro-intestinal tract. Dieulafoy indicates this by the use of the phrase "mucous, membranous, and sabulous entero-typhlo-colitis." This draws attention to the frequency with which sand is passed, and to the fact that the small intestine and cæcum as well as the colon have their share in this disease. Biliary disorders are also common.

This probably explains the beneficial effect on this disease of drinking the Harrogate strong sulphur water. This water taken hot on an empty stomach before breakfast has a prompt aperient action and seldom causes griping. It usually produces one or two loose stools within an hour of being taken and does not, as a rule, cause further action of the bowel during the day. This water increases the flow of bile, which is important in view of the fact that some sufferers from mucous colitis are unable to digest fats.

But it is for intestinal lavage that the Harrogate waters are most useful in mucous colitis. For this purpose two waters are used, either saline sulphur water, or the Harlow Car water of the alkaline sulphur group. The saline sulphur water used in Harrogate for intestinal lavage is a mixture of the yield of several saline sulphur wells, containing in total solids the equivalent of 0·75% sodium chloride, compared with the 0·9% sodium chloride content of physiological normal saline. I think it is often assumed that the water from the Old Sulphur Well, which has a

tonicity of 1·5%, is used for intestinal lavage, and this error may account for the fears which are sometimes expressed that the Harrogate sulphur waters might cause irritation of an inflamed bowel, which as an actual fact very seldom occurs, even when the saline sulphur water is used. The Harrogate water most commonly used for intestinal lavage is, however, the Harlow Car water, which contains in total solids the equivalent of only 0·062% sodium chloride, and as regards tonicity stands between the Buxton thermal water with a tonicity of 0·04%, and the Bath thermal water with a tonicity of 0·24%. That the tonicity of solutions applied to mucous membranes is of importance is evident to anyone who has practised nasal douching, and when I prescribe intestinal lavage for home use I recommend a solution of 1 drachm each of sodium chloride and sodium bicarbonate in a quart of water, which gives a tonicity of 0·63%.

Various suggestions have been made to explain the efficacy of the Harrogate waters in the treatment of colitis, but that they do loosen mucus and casts and soothe inflamed mucous membrane is beyond doubt. The work of Woodmansey and Lissimore shows that they have an antiseptic action on the intestinal flora. This was attributed to the sulphide content. All these waters are alkaline and Mr. Woodmansey tells me that alkaline-solutions of sulphide are used in tanneries for softening and loosening the hair on hides; thus it is possible that even the mild degree of alkalinity of these sulphide-containing waters explains the undoubted clinical finding that they are more effective than plain water in loosening scybala, casts and mucus. The average alkalinity of these waters calculated as sodium carbonate, and using methyl orange as the indicator, is 45 per 100,000. This is of course too mild a degree of alkalinity to irritate mucous membrane.

The things that matter most in giving intestinal lavage are the composition, temperature, amount, pressure and frequency of the injection and the skill and personality of the person administering the treatment.

I have already mentioned the importance of tonicity. I have little personal experience of the use of injections other than those of the Harrogate spa waters and simple saline solutions, but only this month I saw a patient with a very acute mucous colitis who had previously been ordered injections of dilute argyrol solution. These had set up pain and spasm which was at once allayed by the alkaline sulphur water alone.

A temperature of 104° F. in the douche-can ensures the water reaching the bowel just comfortably warm if the tubing is not too long.

The volume of the injection is very important and it should be a rule to check the flow immediately when pain is felt. This may occur after only a few ounces have been injected if there is much spasm. The patient should be allowed to evacuate if the pain persists and the injection may then be cautiously continued. Attempts to overcome the spasm by increasing the pressure only increase pain and should never be made.

I never order more than 40 oz. and usually commence with 25 or 30 oz. at an elevation not exceeding 2 ft. The injection is given with the patient lying on the right side where he remains for two minutes after it is completed. He then turns on the back for two minutes and finally lies on the left side for two minutes before getting into the sitting position to evacuate. At least ten minutes should be allowed for this purpose and the whole process is then repeated. The first wash-out clears away most of the fæces, and mucus when present, thus allowing the second injection to get into more intimate contact with the mucous membrane. As regards frequency it is quite enough if the intestinal lavage be given on alternate days and it is rarely necessary, or wise, to give more than a dozen treatments in one series. Undue prolongation of the course may cause general debility and aggravate nervous symptoms.

In the Harrogate treatment of mucous colitis the intestinal lavage is frequently followed by an immersion bath at a temperature of 102° F., terminating with the application of an undercurrent rose-douche over the abdomen and lumbar regions at 110° F. This at once allays any discomfort that may have been caused by the lavage and also relieves the feelings of cramp or spasm, soreness, and backache that are complained of by so many sufferers from colitis. The bath is followed by a warm towel pack and the patient is then advised to rest quietly at home until the time for the next meal.

Now a final word about the nurses or attendants who administer the treatment. One of our retired attendants who had been in the intestinal lavage department for twenty-five years, and who was highly skilled in her technique and handling of the patients, emphasizes the importance of the following points: The gentle insertion of a well-lubricated rubber rectal tube, carefully avoiding piles and fissures, the detection of spasm by a hand on the patient's abdomen, holding the tube between the thumb and fingers throughout the injection so that the flow can be instantly slowed or checked if colic occurs, and allowing the patient to evacuate at once and rest a few minutes till spasm passes off if the injection causes any pain. She also emphasizes the need for constant watchfulness during the whole time any injection is being given.

Contrasting this gentle handling with the efforts of an unskilled nurse using a Higginson's syringe or a douche-can held well up to ensure a quick flow, there is little wonder that many patients after the latter experience become convinced that they cannot bear intestinal injections. Probably only those who have had enemata for the relief of ileus following an abdominal operation know the agony that can be caused by this means.

Of the intestinal douches given in Harrogate a large proportion are given as part of a detoxicating régime in the treatment of rheumatism. Mucous colitis is often revealed, and just as in the use of salicylates, so in the use of intestinal lavage, the state of the bowel and the joints often improves simultaneously. Not infrequently this improvement follows or is accelerated by the expulsion of a cast, or masses of foul stringy mucus.

I have often been asked whether there is not a risk of causing permanent dilatation or atony of the colon by the use of intestinal lavage. There is certainly no such risk from the brief courses and with the quantities I have indicated, but in this connexion a skiagram I have here may be of interest. [Skiagram exhibited.] The patient had washed himself out with a quart of water regularly, without missing a day, for a period of two years. The skiagram shows the colon to be in a state of spasm, not of dilatation. This was the worst case of oxaluria I have seen or heard of, and the daily lavage of the bowel was the only thing which controlled it.

It has been said that intestinal lavage is more likely to cause than to cure colitis. Whilst this may be true when irritating substances such as soap and turpentine are used in enemata, or when the technique of administration is faulty, intestinal lavage with suitable waters followed by warm immersion baths with hyperthermal undercurrent douching is often most helpful in clearing up the condition in obstinate cases.

Dr. Julius Burnford: I agree with all Dr. Hurst said, and recognize all the conditions associated with mucus which Dr. Hurst put before us. We avoid the danger of overlooking neoplasms and other things which produce mucus, inasmuch as cases which are labelled "mucous colitis" come with a long history of the condition. I presume we are discussing the condition of spasm preceded by constipation, and followed, often—and relieved—by diarrhœa and the passage of mucus, generally in the form of casts. But it is not colitis as there is no

inflammation, and mucus is not a pathological discharge from the colon. I would have liked to hear Dr. Hurst discuss further the normal occurrence of mucus in the bowel, how far it is salutary in the bowel, and especially the state of affairs when a patient enters on a lifelong addiction to colonic lavage. This syndrome is not common. Strange to say, other and definite varieties of inflammation of the colon seem to be getting more and more frequent; the group which comes under the term "ulcerative colitis"—a vague term—and which is characterized by an inflammatory flux, is more common. I am now treating my hundredth case of colitis of the ulcerative form, and I know that others are also having large numbers of these cases. Are we to argue that mucous colitis is a precedent stage of catarrhal colitis? That is a difficult question to answer. Experience suggests that it is in no way allied to the inflammatory group.

Knowledge of anatomical factors in a disease which is not fatal is lacking; we have not the opportunity of the pathologist or of the surgeon to lay down an anatomical basis for the condition we try to define as mucous colitis or mucous colic, so we must argue from symptoms and must deal empirically with those symptoms, regardless of our ignorance as to whether mucous colitis is a distinct state or not.

What is the nature of this mucous colitis? Is it allergic, and allied to the asthmas? Truly, after long months of close application to treatment, some indiscretion in diet may upset the result of all one's well-planned régime. But I hold it is no specific indiscretion, such as it would be if it were allergic. Is it a perversion of function? Putting it in that vague manner, I think we should be compelled to answer "Yes." Is it a true lesion of the colon on which we should focus our attention, or is it a local disturbance the result of a general perverted state?

Finally, what is constipation? Dr. Hurst has pleased me by his elaboration of the idea of stasis and copræmia.

If we do not know what mucous colitis is, how can we approach treatment? Merely on symptomatic principles? Our first duty is to relieve symptoms; then try to ascertain the reason for them and set about eradicating the cause. We have to relieve the pain and the spasm. I have never found them disappear under belladonna; nothing short of morphia is efficacious, with massage sometimes, and with olive oil sometimes. For the constipation I have always preferred an initial dose of castor oil, with laudanum to try to relieve the spasm. But this is the crux of the whole problem: the story of the abuse of the bowel by purgatives, the deep-rooted obsession that if the bowels are not opened daily—even, according to some, tri-daily—the patient has dangerous constipation. I have tried to find some authority for this ritual among earlier physicians or recent ones. Earlier physicians agree that there is no authority for insisting on this regular daily ritual. I do not understand why mucous colitis has not been steadily on the increase when we remember the abuse of purgatives and the abuse of the ancient aloes.

With regard to enemas, I am ill-repaying your invitation to speak by expressing my strong views against colon lavage, and these "colon laundries" of which Dr. Hurst has spoken. I ask "Must the colon be emptied? Must its mucus be got away? Must the benevolent flora of the intestine be washed out? Must the colon muscle be spared the performance of its duty by the taking of drugs and by vicarious washings?" I doubt it. I have had patients returned to me after months of colon lavage with no result evident. Perhaps the patients have had some comfort at the time of the lavage, but no permanent results, and it is these latter we must aim at.

Now after this criticism of modern fashions, what shall I suggest for the relief of the patient? How can we correct the errors? How can we correct the faulty

filling of the colon at one end, and the faulty emptying of it at the other end? For one is probably the result of the other.

First among my suggestions is one concerning diet. My experience is that the article of diet primarily at fault is starch. Fermentation must be avoided and the putrefaction which so often follows or accompanies it. The diet must be bulky, and one would prefer to obtain the necessary proteins in a diluted form more from vegetables, the original food of mankind. They would give the colon its necessary bulk. I have not heard, this afternoon, any adverse comment on "roughage." The bogie of "roughage" has been before us for the greater part of a generation; I do not see how roughage can affect the colon by the time it has passed through the stomach and small intestine; I remember when typhoid fever patients were given only a milk diet, because it was held that more solid food would be detrimental to the ulcerated intestine; yet one saw time after time at autopsy a purely milk diet resulting in the presence of hard, undigested masses of curd in the bowel, which must have been more detrimental than any of the soft semi-digested masses of pulpy roughage. So I have not hesitated, even in my large series of more dangerous cases of ulcerative colitis, to give, from the first, a highly vegetarian diet, and even a roughage diet.

If mucous colitis is a result of faulty action of the colon, it is, in great part, the result of a faulty supply of contents to the colon, and we can get over that difficulty by accustoming the patient to a satisfactory solid and bulky diet. Remember, in doing this, the slow adaptability of the human system; remember the experiment of Pavlov in the "'nineties," and do not be disappointed if the response to the roughage diet is not immediate or even if there be discomfort. Remember also the varying capacity of the colon. One adds to the bulky diet agar agar or the more elegant substitutes, *isogel* or *normocol* to increase the bulk; also some oily product like petroleum or its preparations, but no purgatives.

Secondary to diet, but still of great importance, I place physical treatment. I mean physical measures directed to developing the musculature of the body, to repair particularly the abdominal muscles; particularly abdominal exercises. We must also remember the time factor, for it takes a long period and much patience to train these unaccustomed muscles. As to electrical treatment I will merely say that in every case of mucous colitis in which I have tried ionization, I have not had a gratifying reponse, such as occurs in some cases of ulcerative colitis.

What is the result of this line of treatment? How do we know that it is satisfactory? The answer is, that the patient begins to pass, at the intervals which are peculiar to him, well-formed stools, not scybala, but somewhat solid, and inodorous—proving that there is no putrefaction—and then there is no indican in the urine. Such a normal state speaks for cure, and if it is maintained with the co-operation of the patient the treatment should be successful.

Dr. E. I. Spriggs said that mucous colitis, as practitioners knew it, was a clinical entity, and it was due mainly to two things: (1) constipation, (2) the regular use of aperients with the object of curing the constipation. The second of these factors he regarded as the more potent. He founded that statement on figures. He asked Dr. Picton-Davies to go through the notes of 1,000 cases of delay in intestinal contents as tested by X-rays. If much material remained in the ascending colon and cæcum on the first morning after a motion, it was termed "slight delay." If after seventy-two hours following a motion there was much material in the distal part of the colon, that was definite delay. In the 1,000 cases of definite delay, 236 people did not complain of constipation, and they had not taken aperients. The remainder of the 1,000 did complain of constipation, and of

those, six out of every seven were taking aperients constantly. Nearly 500 were taking them every day. What was the incidence of mucous colitis in that series? The diagnosis was made at the beginning of observation of the patient, before any treatment such as lavage was applied. The incidence in those complaining of constipation and who took aperients was more than twice that of those who had constipation alone.

With regard to the frequency of mucous colitis in 4,000 consecutive cases, 157 were diagnosed as having mucous colitis, after a complete examination was made. Many others passed mucus and had disorders of the colon, but in them those events were regarded as secondary to some other condition. Of these 157, 13 had severe muco-membranous colitis. Of 47 consecutive mucous colitis cases complaining of diarrhœa, in all but nine there was delay in the bowel contents; they were suffering from constipation and were passing fæces mixed with mucus, and as the motions were soft and unformed, they considered they had diarrhœa.

The importance of a correct diagnosis had been mentioned by Dr. Hurst, and to the two interesting cases quoted by him, he (Dr. Spriggs) would like to add another.

A man complained for eleven years of intermittently passing mucus; he also had discomfort, sometimes amounting to pain, in the left loin. He was treated for mucous colitis, and two and half years before he (Dr. Spriggs) saw him he had been examined by X-rays, and the diagnosis of mucous colitis confirmed. Pain and the passage of mucus became more severe, and occasionally a cast of mucus 9 in. long was passed. When the speaker saw him a stone was shown to lie in the left kidney. After its removal he had no more pain, and no more mucus was passed. Ten years later his mucous colitis had not recurred. It was clearly reflex.

With regard to the frequency of achlorhydric gastritis, in the series of cases that he mentioned, in 242 cases of functional disorder of the colon, there were 2% with achlorhydria of the 111 cases examined with a test-meal. He would not classify an achlorhydric looseness under the heading of mucous colitis. 43% of the 111 patients had superacidity, 23% had subacidity.

Again this evening the term "colitis" had been attacked; it was not the first time, for frontal movements against the term had been going on ever since the condition was first fully described in 1888 by Sir William Hale-White. One suggestion from America was "spasmo-myxorrhœa."

Dr. Hurst's remarks on mucous secretion being stimulated by douches went further than he (Dr. Spriggs) would when he said that douching, even when not excessive, was a common cause of the disease under discussion. Two French physicians, Chiray and Stieffel, stated that muco-membranous colitis was caused by washing out the bowel. That statement Dr. Spriggs characterized as in many cases not so. If one went on douching out the bowel, gently and carefully, the quantity of mucus passed became progressively less, and after a dozen douchings with isotonic solution it ceased. Amateurs would point to this diminution and final cessation and say, "See, we have cured you." The explanation, however, was that the bowel had become tolerant, as well as, in diseased bowels, healthier.

He followed up a series of patients who had come with a suggested diagnosis of intestinal auto-intoxication. In 50% of those cases there was an organic lesion in the abdomen—appendix, gall-bladder, etc.—and in many of the rest the main trouble was neurasthenia.

With regard to diet, in most cases of mucous colitis the patients could bear a fairly rough diet, i.e. one containing solids and fruits, and, if borne, it would do good. If not, a bland diet should be given to begin with. Professor Boas, of Berlin, reported that during the War mucous colitis and muco-membranous colitis had

almost vanished from Berlin. At that time they were very short of meat, and had to rely greatly on vegetables and substitutes.

Dr. Kerr Russell said he would like to know what particular method of colonic irrigation Dr. Burnford administered or prescribed, as that speaker had said that he had never seen any good follow it, and this was quite contrary to his (Dr. Kerr Russell's) own experience. There were a number of different methods of colonic irrigation, some good and some bad.

In muco-membranous colic there was a spasm of the bowel musculature, and that spasm could be relieved by the application of heat. The injection of a hot solution often gave relief, apart altogether from the mechanical clearing out of the bowel which resulted.

Dr. Burnford spoke of "this modern fashion of irrigation" but a glance through old medical works showed that colonic irrigation was given hundreds of years ago.

Dr. Hurst had mentioned the value of diathermy in rectal conditions. It should be remembered, however, that the essential feature of diathermy was the production of heat. He suggested that localized internal heating could also be obtained by the use of hot irrigating solutions.

Dr. Burnford (in reply to Dr. Kerr Russell) said that his reference had been to patients who had been away to spas and had returned no better for their lavage. Probably at the time when the lavage was given they had felt improved, but the improvement was temporary.

Dr. G. B. Batten said that he remembered Sir William Hale-White making an investigation, thirty-five years ago, into the treatment of what was still called muco-membranous colitis. Among other treatments, Sir William had asked him and others to try high-frequency currents for it. He (the speaker) had been using these ever since he had an electric installation at his house in 1896. He treated the condition by effluve on the abdomen, and by the rectal application of a glass electrode, of the shape Dr. Hurst had shown—both on a condenser couch. He was gratified to find this was a successful treatment for hæmorrhoids also. Incidentally he found this treatment was good for other conditions such as what patients called constipation and for insomnia. He now used diathermy in the same way.

With regard to the lessening incidence of muco-membranous colitis, in general practice, before the European War, patients used to consult him because, they said, they had passed a worm; usually they were the neurotic type of people, who had observed pieces of so-called membrane when they went to stool. He had seen very few cases of that kind during the last fifteen years.

With regard to ulcerative colitis: A young woman, whose parents kept a small shop, had this disease very definitely. She was very thin, and when she came to him (the speaker) she used to pass from a pint to a quart of pus a day. He put her on to a strict diet chiefly of milk and eggs. Her family insisted on having a particular nurse. The patient grew steadily worse, and eventually she became so ill that her former doctor saw her in consultation with himself (Dr. Batten). They agreed that she was not likely to live another week, and her parents then asked whether they might give her what diet they liked, and this was agreed to. This meant the dismissal of the nurse, and from that time the patient began to get better and eventually quite well. It was found afterwards that the nurse had been in the habit of bringing port wine, jelly and other foods, and when the patient could

not take them the nurse had taken them herself! This patient had since married and had children.

About twenty-five years ago he had heard a vivid discussion at the Section of Electro-Therapeutics on the treatment of intestinal stasis, and he congratulated Dr. Hurst on sticking to his guns. Dr. Hurst had said, on that occasion, that he did not believe in intoxication due to stasis, and in support of his view had shown a large series of skiagrams.

Section of Ophthalmology

President—A. C. HUDSON, F.R.C.S.

[*December* 8, *continued*]

Two Cases of Ocular Tumour.—R. LINDSAY REA, F.R.C.S.

(I) *Intra-ocular.*—In June 1933, I saw a patient, aged 77, who had told me a few weeks previously that she had been seen locally and had been informed that a small spot on her iris was probably a malignant growth.

Radium treatment had been prescribed but the only result from this, apparently, was a stubborn conjunctivitis.

I examined the eye with the slit-lamp and could see in the grey iris, at 6 o'clock, not only a brown area which was apparently part of a small tumour, but immediately outside it a few scattered brown patches (see Plate). Upon dilatation the iris retracted freely, without synechiæ being present. Also iritis was not present.

I came to the conclusion that this was a sarcoma of the iris which was already beginning to spread.

The eye was removed and a microscopic section was made (see Plate). The growth proved to be a spindle-celled sarcoma.

In this case, the growth occupied the middle sixth of the iris below and did not reach to the ciliary body. Some of the small vessels and the lymphatics in the immediate neighbourhood of the growth were filled with sarcoma cells but the vessels of the ciliary body and the sclerotic appeared to be free.

The corneal microscope and slit-lamp aided considerably in the diagnosis, as the brown patches spreading in the iris were readily distinguished.

(II) *Extra-ocular.*—The second case is that of a man, aged 64, whom I saw in September 1933, on account of what appeared to be a small fatty tumour above the right eye, lying on the insertion of the superior rectus muscle. This man from birth had been a tuberculous subject and this tumour had appeared recently. I tried to aspirate it, thinking only of a tuberculous abscess, but I found it to be solid. The conjunctiva was reflected back quite easily under cocaine and the tumour shelled out exactly like a lipoma. The pathological report a few days later stated that it was a round-cell sarcoma. Later it turned out to be a true lymphosarcoma which was a metastasis from a primary lymphosarcoma elsewhere.

The treatment for these tumours is deep X-ray therapy, not radium, and so I at once got into communication with the patient's relatives and discovered that he was exceedingly ill from some obscure abdominal cause, and also that phlegm was being brought from the chest.

I came to the conclusion that the man was probably in the last stages of suffering from pressure from the original tumour and that therefore further treatment would be useless. To my surprise, however, I was asked to go and see him at the beginning of this month. I found him very weak and the eye completely enveloped by a recurring growth which had extruded it outside the orbit. The pain was intense.

The patient begged me to do what I could. I rendered the nerves within the orbit insensitive with novocain, and as the tumour was not adherent to the periosteum, I shelled it out quite easily with the eye embedded within it. The patient made an uneventful recovery.

Now it is found that the primary growth was in the spleen and is extending half-way across the abdomen. The patient is, however, entirely free from pain.

Summarized Reports of Eight Cases of Coloboma of Iris and Choroid (Congenital).—A. HUGH THOMPSON, F.R.C.S.

Sex.—Three male, five female (all under age of 18).

Direction of coloboma.—Four cases directly downwards ; four cases downwards and slightly inwards.

Nystagmus.—Four present ; four absent.

Microphthalmos.—Three out of eight had one or both eyes small.

Myopia was present in ten out of thirteen eyes.

Vision.—Out of fourteen eyes tested, nine had various degrees of blindness from $\frac{3}{60}$ down. Three eyes had $\frac{6}{60}$; two eyes had $\frac{6}{36}$.

Two Cases illustrating Defective Form and Colour Vision (Familial).—STEWART MACKY, M.B. (introduced by Mr. RUGG-GUNN).

(I) H. H., male, aged 14, a factory hand.

History.—Failing vision, not improved with glasses. Dry skin since he was a baby. In 1926 right vision=$\frac{6}{60}$, not improved; left vision $\frac{6}{36}$, not improved. No family history of poor vision except in his younger brother.

On examination.—Right eye $\frac{6}{60}$, left eye $\frac{6}{36}$; not improved. Pupils equal and active. Media clear. Fundi normal, except that the foveæ are highly refractile.

Perimeter fields.—Form full, colour greatly contracted, while red is called "brown" and green "yellow."

General ichthyosis with double ectropion. (This is inherited from his mother.)

(II) J. H., male, aged 8.

History.—Poor vision like his elder brother. No other family history.

Examination.—Right eye, vision = $\frac{6}{60}$, with $-$ 1·25 sph. $+$ 0·78 cyl. axis 120° = $\frac{6}{18}$. Left eye, vision = $\frac{6}{36}$, with $+$ 0·75 sph. $+$ 0·75 cyl. axis 90° = $\frac{6}{24}$. Fundi rather peppery and tigroid. Wassermann reaction negative.

Fields.—Concentrically contracted for form and colour.

Embolism of Left Ophthalmic Artery.—T. C. SUMMERS, F.R.C.S.

Patient, G. G. T., a boy, aged 7 years. Four and a half months ago, transient erythematous rash over body; general malaise; duration three or four days.

Four months ago, return of general malaise; severe headache, vomiting and puffiness of the eyes. On the following day the face became very swollen and he passed deep red urine. Remained in bed for five weeks, improving all the time.

Three months ago, severe headache suddenly developed. The doctor was called in and he prescribed some sleeping draught. A few hours later the boy was asleep. On the following morning it was first discovered that he had lost his left vision. During the following two days it was also noticed that the right arm was almost completely paralysed. He had several more attacks of headache but never so severe as on the first occasion. One week later he was able to get up, but his right arm still remained weak. Peeling of hands and feet was noticed at this time.

On examination.—On palpation of the carotid arteries, pulsations are found to be less strong on the left side. Slight hemiplegia. Urine normal. Cerebrospinal fluid normal. Blood-pressure 90/60. Skiagrams of skull negative.

Diagnosis.—Embolism of ophthalmic artery.

The following cases were also shown:—

By H. J. TAGGART, F.R.C.S.—Four Cases of Retinal Detachment operated on by Safar's Method. Six Cases of Modified Motais' Operation for Congenital Ptosis. Phlyctenular Keratitis, with Peculiar Disturbance of the Cervical Sympathetic.

By G. G. PENMAN, F.R.C.S.—Detachment of Retina operated on by Safar's Method.

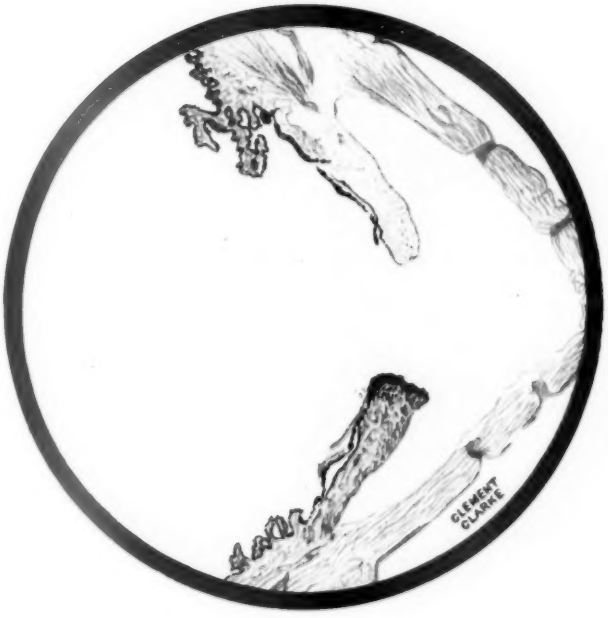
By R. LINDSAY REA, F.R.C.S.—Two Cases of Squint in Young Children after Operation. Neuromyelitis Optica of Devic. Intracranial Tumour (Left Acoustic).

By T. COLLYER SUMMERS, F.R.C.S.—Hyperplasia of Pigment Epithelium following Iridectomy. Drusen. Monocular Retinal Hæmorrhages with Detachment.

By EUGENE WOLFF, F.R.C.S. — Hole at Right Macula. Bilateral Superficial Punctate Keratitis.

Mr. RAYNER D. BATTEN, M.D., gave a Demonstration illustrating Tension (Superficial and Deep) in Air Balloons.

Sarcoma of iris.



Section through tumour showing relation to iris.

R. LINDSAY REA: Intra-ocular Tumour.

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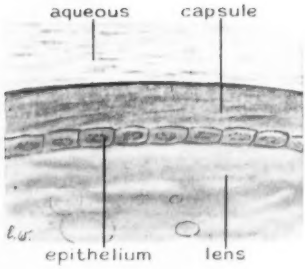

FIG. 2

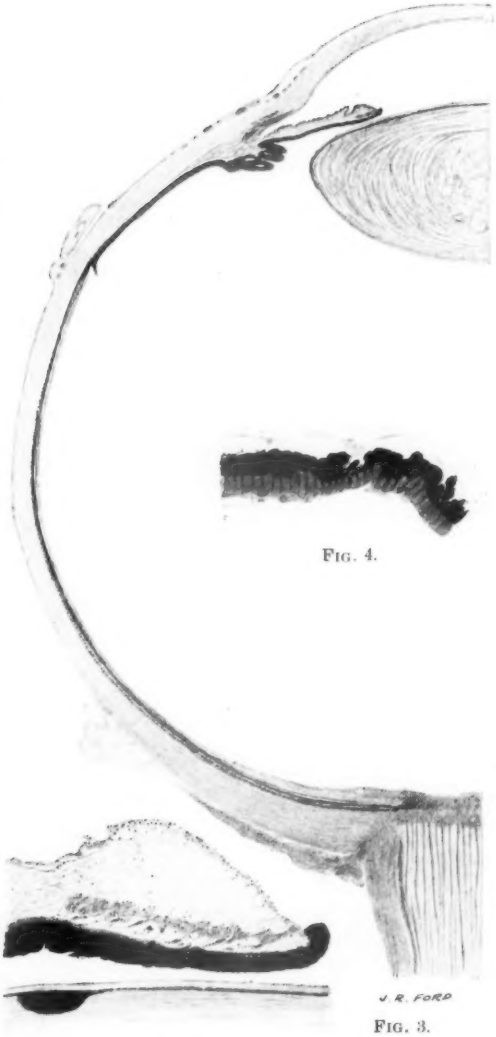

FIG. 3.

FIG. 4.

FIG. 5.

EUGENE WOLFF: The Spread of the Iron Compound in Siderosis Bulbi.

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[*January* 12, 1934]

The Spread of the Iron Compound in Siderosis Bulbi.

By Eugene Wolff, F.R.C.S.

(*From the Pathological Department of the Royal Westminster Ophthalmic Hospital*)

In reading through the various accounts of siderosis bulbi, I found great difficulty in understanding why certain portions of the eye seemed to take up the rust-like substance while others did not.

Some (von Hippel, Parsons, Collins and Mayou) hold that it is because of a special affinity which certain tissues or cells have for the iron.

I do not believe, however, that it is necessary to ascribe a special affinity to certain tissues, except in so far as I think that all living cells will take up the iron more readily than the connective and other tissues and that these again will stain more intensely than the glass-like membranes.

Moreover, I hope to show that for a given size, type and position of the iron particle, the march of events in siderosis bulbi is quite definite, and to do this I would divide the process into three stages.

(1) The latent period. During this period, which may be anything from a few weeks to many years after the injury, the iron is converted into a diffusible compound which stains the tissues around it (direct siderosis of Bunge, fig. 1) and then makes its way into the aqueous or vitreous. Probably the solution of the iron particle will be most rapid when it lies in or is bathed by these fluids and hence also in such cases the latent period will tend to be short.

The exact nature of the iron compound so formed is disputed. Leber held that the iron was dissolved by the carbonic acid of the tissues, carried away as a bicarbonate of the suboxide of iron, and again precipitated in an insoluble form under the influence of the oxygen of the tissues. Bunge held that it was, therefore, very liable to collect round vessels, as is seen in the retina. Others have suggested that the iron is dissolved by acid phosphates or that it may enter into solution in organic form as an albuminate or as a colloid. McMullen found that the brown particles in the tissues did not consist of a simple oxide or hydroxide as they are only slightly soluble in oxalic acid.

Whatever the substance is, I believe it to be diffusible and that it must get into the aqueous or vitreous to produce the complete picture of siderosis bulbi. The vitreous has indeed often been found rust-coloured in this condition.

(2) The second stage is the spread through the intra-ocular fluids, i.e. through the aqueous and vitreous (fig. 1). In doing this the diffusible iron compound stains *all* structures with which it comes into contact so that in the first place all structures bathed by vitreous or aqueous will be affected.

(*a*) The iron compound passes through the lens capsule (fig. 2) and internal limiting membranes; (*b*) it is taken up by all living cells with which it comes into contact and is converted by them into an insoluble compound. Its action on the cells is no doubt at first irritative (as is shown best by the characteristic proliferation of the subcapsular epithelium) and later destructive.

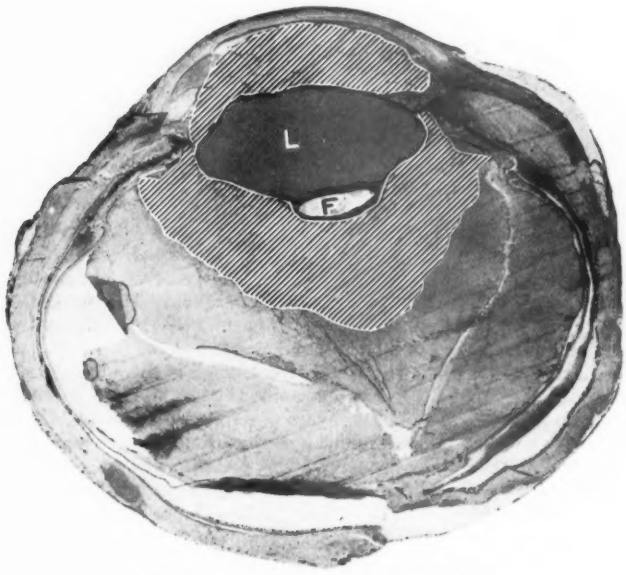
The various portions of the eye will now be taken in turn and the effect of the iron compound on them described.

The ciliary epithelium, bathed by both aqueous and vitreous, will obviously be affected early, because the dye, spreading through these fluids, will pass through the feeble, or in parts non-existing, internal limiting membrane and will be taken up by the living cells constituting the epithelium.

The iris.—Slit-lamp microscopy has taught us that the iris must not be regarded as a membrane, but as a sponge whose meshes open freely into the anterior chamber. Those portions, and more especially the living cells which are bathed by the aqueous, will take up the iron.

Thus Perles' reaction is most marked in the anterior limiting layer (which accounts for the changing of the colour of the iris in the living to brown), in the sphincter and dilatator papillæ.

The lens—its capsule, suspensory ligament and epithelium.—The capsule: In a case (figs. 1 and 2) where the eye was removed sixteen days after the entry of a piece of steel, for severe inflammation and retained foreign body, the capsule stained blue



L = Lens. F = Position of foreign body.

FIG. 1.—From an early case of siderosis bulbi: the eye was removed sixteen days after the entry of the iron. The barred area shows the spread of the iron compound through the vitreous and aqueous, as shown by Perles' reaction. The foreign body was lying in the vitreous behind the lens, which was wounded.

with Perles' reaction. This case is especially interesting as it shows that the iron is actually passing through the capsule, for the epithelium does not yet stain blue (fig. 1).

It is probable that here the concentration of the iron compound was greater than is usual in cases of siderosis bulbi, for there is no other record, so far as I am aware, of the capsule staining blue with Perles' method. (Potassium ferrocyanide and hydrochloric acid.)

But since the compound must necessarily pass through the capsule to reach the epithelium of the lens, it seems obvious that it must contain iron in every case where the epithelium is affected and the process of siderosis is actively proceeding. That it is not usually seen is no doubt due to the fact that Perles' reaction is not delicate enough to show up such small quantities of iron.

The suspensory ligament: In the above case the suspensory ligament stained faintly, but I think quite definitely, blue with Perles' method, and here again I believe that if the test be delicate enough iron could always be demonstrated in it in cases of siderosis bulbi.

The epithelium of the lens consisting of living cells takes up the compound very readily, and no doubt owing to its irritative action they proliferate in places, and thus are formed under the lens capsule the characteristic brown patches which are pathognomonic of siderosis bulbi (figs. 3 and 5). These patches usually form a ring which is just beyond the contracted pupil (fig. 5) (i.e. the pupil has to be dilated to see them properly). This site of predilection may be due, perhaps, to a concentration or stagnation[1] of the dye in the posterior chamber behind the angle formed by the iris (in contact with the front of the lens) and the lens capsule; or it may be that the attachment of the suspensory ligament further laterally acts as a partial barrier. The iron compound gradually diffuses through the lens.

The angle of the anterior chamber and cornea.—The ligamentum pectinatum is readily affected because the aqueous drains through this. The living cells on the trabeculæ will take up the iron more readily than the other portions. The iron compound diffuses through the cornea, mainly from the region of the angle, affecting the substantia propria, and more especially the corneal corpuscles. Eventually the corneal epithelium is also affected (fig. 3).

The retina.—Here again the iron compound passes from the vitreous through the internal limiting membrane and the nerve-fibres, affecting these slightly, and is taken up by the ganglion cells and later by the other layers of the retina. That the retina is affected from the side of the vitreous is strikingly shown by a case of Morax figured in his "Pathologie Oculaire," Plate IV (fig. 3), where the retina to the ganglion cell layer is affected and the remainder hardly if at all. Eventually, however, the whole retina is involved.

The choroid is but little affected, for the iron compound has to pass through the retina to reach it. In this there is a pathological analogy with panophthalmitis, where the vitreous may be full of pus and the choroid but hardly affected, for here too the toxin (or bacteria) has to pass from the vitreous through the retina to reach it.

The sclera will no doubt be affected if the process goes on long enough.

(3) The third stage marks the further effects of the iron compound especially on the retina.

The ganglion cells and other nervous elements of the retina degenerate and the glia proliferates. The pigment epithelial cells which readily take up the iron proliferate, become mobile, invade the retina and tend especially to collect around the vessels. Thus is produced a picture which closely resembles that of pigmentary degeneration of the retina and, indeed, night-blindness and contraction of the field of vision are characteristic of the later stages of siderosis bulbi. Finally the retina may become detached. The lens becomes opaque, and it is possible that changes in the ciliary body may give rise to a more albuminous dialysate and produce the rise of tension seen in some cases.

Summary.—Thus we see that, in siderosis bulbi, there is a latent period which may extend from a few weeks to many years, during which the iron is dissolved, and the diffusible compound so formed makes its way into the aqueous or vitreous humour. It follows from this that the siderosis bulbi will be most rapid where the iron particle lies in or projects into these fluids.

Next comes the spread through the intra-ocular fluids and the staining of all structures bathed by these fluids. This I believe to be quite rapid, for one may be

[1] Since the flow of aqueous from the posterior chamber to the anterior is very slow and probably intermittent.

surprised to see the particles under the lens capsule which were not present at a visit only some days before.

Lastly come the degenerative changes resulting from the absorption, and seen most characteristically in the retina and lens.

[I wish to thank Mr. Hine and Mr. Penman for the pathological material used in the preparation of this paper, and Mr. W. H. McMullen for a very interesting paper on siderosis bulbi which he wrote many years ago, but, unfortunately, never published.]

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Discussion.—Mr. FRANK JULER said a paper on a similar subject had been published by Mr. Mayou some time ago, in which attention was drawn to the condition of siderosis bulbi, which, the author said, might be due to diffusible iron in colloidal form. (*Trans. Ophth. Soc.*, xlv, 274, and xlvi, 167.)

Mr. WOLFF (in reply) said Mr. Mayou believed that the iron compound was a colloid substance, and unable to get through a semi-permeable membrane like the lens capsule. Mr. Mayou, therefore, held that the capsule had to be injured for the subcapsular epithelium to be affected. He (Mr. Wolff) had shown a section in which the iron was passing through the lens capsule, and therefore he believed that the iron would get through the capsule even though it was not ruptured, i.e. through the intact capsule.

Description of Plate

FIG. 2.—From the same case as fig. 1. The aqueous and capsule of the lens are stained blue by Perles' reaction, but the epithelium does not as yet stain.

FIG. 3.—A typical case of siderosis bulbi stained by Perles' method, counterstained eosin. The foreign body had entered the eye five months before and lodged in the vitreous behind the lens.

FIG. 4.—Same case as fig. 3; enlarged view of the ciliary epithelium.

FIG. 5.—From the same case as fig. 3, to show how the iron collects in the anterior limiting layer of the iris, the sphincter and dilatator pupillæ, and the epithelium of the lens. Note the typical collection of pigment due to proliferation of this epithelium.

Three Groups of Unusual Fundus Disturbances

By ARNOLD SORSBY, F.R.C.S.

I.—*Familial Occurrence of Macular Coloboma associated with Apical Dystrophy of Hands and Feet*

Macular colobomata, as Miss Ida Mann has pointed out [1], can be classified as of three varieties:—

(1) Pigmented; (2) non-pigmented; (3) with associated blood-vessels.

It is generally said that the non-pigmented variety is the commonest, but this is probably not the case.

There is undoubted evidence that some unilateral colobomata of the macula are of inflammatory origin. This explanation is, however, not generally accepted. It is certainly unacceptable for the majority of bilateral colobomata. Most authorities regard these as embryological defects, even though the explanation that held the field for many years—viz., that the macular coloboma represents a failure in the closure of the choroidal cleft before it has rotated round to its normal position—has been proved fallacious. Miss Mann has rejected the various attempts at an explanation on an embryological basis and advocates the view that these colobomata are of inflammatory origin, some from post-natal, others from intra-uterine inflammation.

She holds that the pigmented colobomata represent irritative lesions, and the non-pigmented destructive lesions.

This view as to the inflammatory origin of macular colobomata is seriously challenged by three family groups reported, respectively, by Clausen, Schott, and Davenport.

Clausen [2] reports the presence of bilateral coloboma of the macula in a brother and sister. Two sons of the brother, as also two daughters of the sister, are likewise affected. Schott [3] reports the affection in two daughters of an unaffected man, whose sister was affected. Davenport [4] reports the lesion in a mother and son.

The cases shown to-night constitute an additional group. The mother has bilateral coloboma of the macula. She had seven children, five of whom showed the same defect. The colobomata are of the pigmented variety. The parents are not consanguineous and no macular coloboma could be traced in any members of the mother's family. The Wassermann reaction is negative in the mother and the affected children.

What is of special interest in this group is the associated skeletal defect. This defect conforms to the rare condition described by MacArthur and McCullough [5] as " apical dystrophy of hands and feet." Absence of nails, especially on the index fingers and the big toes, stunting and even absence of phalanges, tendency to bifurcation of the terminal phalanx of the thumb and big toe are present. The two children of this family who are unaffected by macular coloboma show no skeletal defect.

One affected member of this family died a year ago. Unfortunately, an eye could not be obtained for histological examination. The post-mortem findings—for which I am obliged to Dr. M. R. M. Whigham, Medical Superintendent of St. Andrew's Hospital, E.—revealed congenital absence of the left kidney and suprarenal gland.

Apart from the ocular and skeletal defects no lesions could be established in this family. Their intelligence is normal and there is no history of mental deficiency.

(II) *Central and Paracentral Tapeto-retinal Degeneration*

Several distinct types of familial retinal degeneration have been described. There are: (1) Hereditary optic atrophy, of two types—recessive and dominant; (2) Hereditary pigmentary degeneration—the so-called retinitis pigmentosa; (3) Hereditary macular degeneration—in which the lesion is confined to the macula and makes its appearance at different ages in different families, but always at the same time in the same family. Sometimes the lesion is present at birth; at other times it occurs at the second dentition; sometimes in adult life; sometimes at about 45 and even later. Best's disease, Stargardt's disease, and Tay's choroiditis are some of the names applied to this group with its varying age-manifestations.

These groups of localized retinal lesions are to be distinguished from other hereditary groups in which the retinal lesion is merely part of a more widespread process; such as Tay-Sach's disease, Batten-Mayou disease, the Laurence-Moon-Biedl syndrome and others.

The group shown to-night, consisting of six members of one family and of two isolated cases, has some distinguishing features of its own. It is of course familial, and it combines features of the three other groups.

(1) Some cases show optic atrophy. These are probably the most advanced cases of this group.

(2) All show a central lesion, not confined to the macula; in fact, the macula is spared in some cases, though there is much surrounding pigmentary disturbance.

(3) The periphery is clear, though the process extends much further than just the central area.

Though definite ophthalmoscopic lesions are present in all cases, vision is not—as yet—impaired in all the patients. A striking case is the boy showing distinctly

pale discs and a distinct lesion at the maculæ, and yet vision is practically full (6/6 p. each eye). There is no night-blindness in this group—a distinguishing feature from retinitis pigmentosa; the lesion is not confined to the macula, which may indeed be spared; it is distinguished from Leber's atrophy by its gross retinal involvements. The fundus appearance is totally unlike that in Doyne's choroiditis.

Dr. Worster-Drought, who kindly referred to me the first case of this group, has examined several members and reports that there are no associated defects.

(III) *Cavernous Atrophy of Discs associated with Retinal Arteriosclerosis*

The four cases shown to-night would not of themselves justify a plea for a distinct clinical entity. They are, however, representative of a group of ten cases observed during the past two years. The elements of this group are: (1) Advanced retinal arteriosclerosis associated or not with choroidal sclerosis; (2) Optic atrophy of a characteristic type, the dominant feature being cupping. The cupping is definitely not glaucomatous. It is not physiological, for not only is the lamina cribosa seen distinctly but the cupping encroaches on the intermediate zone of the disc. Nor is the cupping of the type which is known as shallow cupping of optic atrophy; it is most distinctly not shallow; (3) Tension is normal, and the fields show uniform (i.e. non-glaucomatous) shrinking; (4) Complications of retinal arteriosclerosis are common. These are most frequently of the nature of occlusion of either the central artery or vein, or some branch. Hæmorrhages and exudates are of subsidiary significance and frequency; (5) The final stage in seven out of twenty eyes has been acute glaucoma.

A characteristic history is the following:—

Patient, aged 74. Seen two years ago. Vision $\frac{5}{6}$ each eye. Cavernous cupping, atrophic discs and advanced retinal arteriosclerosis. Tension normal. Fields not glaucomatous.

On a second visit, two months later, occlusion of a branch of the inferior temporal artery in the right eye, and thrombosis of a branch of the inferior temporal vein in the left were observed. The patient did not attend any more.

On re-examination ten days ago, the left eye was found in a state of absolute glaucoma following an acute attack last June. Vision with the right is now P.L. Tension normal.

The term cavernous atrophy has been applied to the rather characteristic cupping in this group of cases. It would probably have been wiser to avoid it, as it suggests that this group of cases is like that described by Mr. Ransom Pickard. His cases, however, show typical glaucomatous cupping, not produced by increased tension and not showing the features and course of glaucoma. In the group shown to-night there is no glaucomatous cupping until the supervention of glaucoma.

At this stage it is perhaps uncalled for to discuss the mechanism of the formation of cupping in these cases. It is certainly not produced by increased tension. Might I suggest that the arterial sclerosis is present in the ophthalmic artery and that contraction along its adventitia pulls the lamina backwards?

I submit for your criticism the suggestion that some cases of so-called acute primary glaucoma in old people are simply manifestations of the terminal stage of a process which has characteristic features of its own, namely, optic atrophy with distinctive cavernous cupping, associated with retinal arteriosclerosis and its complications. The condition shows none of the features of chronic glaucoma; it is bilateral and its prognostic significance to vision is grave.

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DETAILS OF ILLUSTRATIVE CASES

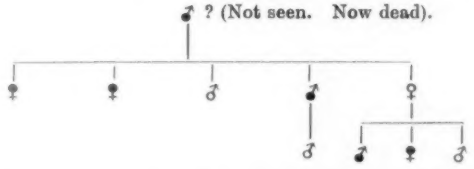
I.—A family group consisting of a mother and four children.

All show large bilateral "macular coloboma."

There is also present terminal dystrophy of hands and feet, as shown by (1) defect in the nails on the index fingers and first or second toes; (2) stunting or suppression of terminal phalanges; (3) varying deformity of terminal phalanx of thumb and big toe, ranging up to bifurcation. A sixth member of this family showing these changes to the greatest extent died in January 1933. Fundus drawings and X-ray photographs relating to him are shown. The father and two children of this family are normal. Family history negative. No consanguinity.

II.—(1) A family group consisting of three sisters, one brother, and two of the three children of one of the sisters.

This group illustrates a defect which ranges from mild pigmentary disturbance to extreme atrophy in the central area associated with discs ranging from normality to complete atrophy. Vision ranges from $\frac{6}{6}$ to P.L. There is no pigmentary disturbance in the periphery. No night-blindness. There is an unaffected brother in this family. The affected brother has a normal child. The third child of the married sister is normal. Wassermann reaction negative. The father of the first generation became slowly blind in middle life. No consanguinity between the parents.



(2) Two unrelated cases showing the same condition. The girl is blind (P.L.). The boy has $\frac{6}{6}$ vision.

III.—Illustrating the varying stages in the complications of cavernous atrophy in retinal arteriosclerosis.

(1) The earliest stage consists subjectively of failing vision, objectively of pale discs with clear margins and an exaggerated physiological cup. The cup is not of the shallow type of optic atrophy, nor of the glaucoma type and no signs of glaucoma are present. Marked retinal arteriosclerosis is present.

(2) Subsequently the complications of retinal arteriosclerosis develop, localized thrombosis of arteries and veins being the commonest. Isolated hæmorrhages and exudates are relatively infrequent.

(3) The terminal stage is frequently secondary glaucoma.

Discussion.—Miss IDA MANN, referring to the first group of cases, said that she was not aware of any name having yet been given to this type of case, but all the cases were so similar that it seemed right that they should bear the name of a definite syndrome. She did not know whether the association of macular colobomata with deformities of the extremities had ever been pointed out before.

There could be no question that these abnormalities were developmental in origin; the fault must lie in the germ plasm, and it was an interesting embryological exercise to attempt to establish a connexion between the developmental failure in the bones of the extremities with the macular condition. At first it seemed almost impossible to see any connexion; one thought, "Here is a mesoblastic failure involving the extremities and also a failure in the optic cup which is epiblastic, and it is impossible embryologically to connect the two." But on looking more closely into the matter, she had come to the conclusion that the failure in the eye was also entirely mesoblastic. The fault, she thought, was choroidal, not retinal, because of the large number of places in which one could trace the retinal vessels

unchanged over the area of pigmentary disturbance. That, therefore, did not make it so inexplicable as would an epiblastic failure linked with a mesoblastic one.

This series also had an important bearing on genetics. It might be thought to show that there existed a separate genetic factor for the development of different parts of the choroid. It would have been of added interest if skiagrams could have been shown of the complete bodies of some at least of these patients, so that it could be seen whether the abnormalities embraced other mesodermal structures, such as the ribs, vertebræ, and long bones generally.

With regard to the posterior pole of the choroid being a separate genetic entity, she did not know of any other evidence in favour of that except the unconvincing evidence of comparative anatomy. One found in certain other species, not related to man, specializations of various parts of the choroid, which meant that the choroid developed in areas in those animals. An instance was the choroidal gland, a thick mass of blood-vessels at the posterior pole in teleosteans. In mammals also specializations connected with tapetal areas occurred in some species.

Hence, there might be a representation in the genes of definite areas, and these cases now shown might be instances of a failure of the gene which governed the specialization of the posterior pole.

It was interesting to see the two sets of cases, side by side, since the second set appeared to be an involvement of the ectodermal elements alone, and formed an instructive contrast.

Dr. E. A. COCKAYNE said that from the genetic point of view he regarded this as a most important family. He did not, however, think that it was necessary to believe that the defect in the eye was in any way associated with the skeletal one; he could not see any objection to regarding this as an instance of linkage of two unrelated defects, both appearing first in the mother. It was possible that one of that mother's parents, instead of having one mutation in a germ-cell, had two mutations affecting two independent genes in the same chromosome. If so, both the defects were bound to be transferred together to every affected member since they were carried in the same chromosome, unless crossing-over took place.

In man, few examples of linkage were on record. There was the Laurence-Moon-Biedl, in which there was recessive polydactyly which occurred fairly commonly without the retinal defect, which he thought was probably due to another gene altogether. The skeletal defect in the family shown to-night, he thought, must be extremely rare. These defects of hands and feet had never been properly classified or named, and so were not indexed in the periodicals, and it was an almost superhuman task to try to find records of examples of any particular defect of the bones of the hands and feet. He did not know of another example quite like this. He had looked up many examples of nail defects, but none were associated with the duplication of the terminal phalanx and the absence or diminution of one of the phalanges of the fingers. There was a condition in which nail defect accompanied absence of patella or a small patella.

Mr. R. AFFLECK GREEVES said he would like to show, for another Member, a picture of a unilateral coloboma identical in appearance with those shown by Mr. Sorsby. [Slide exhibited]. The patient was a man, aged 38, whose other eye was normal. The history was that he had sustained a blow with a cricket stump when 10 years of age; the sight was said to have been good before that accident but had been defective since. It was possible, however, that the defect was present before but had not been noticed. Still, there was the suggestion that this kind of unilateral macular coloboma might result from an injury.

Mr. RANSOM PICKARD said that he wished to say a few words about glaucoma and cavernous atrophy. He had worked for some years on the question of this apparent glaucoma occurring without rise of tension, and had been trying to devise ways of distinguishing it from glaucoma by means of various tests, though so far in vain. The only difference which he could find between them was that glaucoma had a raised tension, while cavernous atrophy had not. That brought in the question of the standard of normality. That standard permitted of a good deal of latitude, but it was so important that he had such patients come to see him early in the morning and late at night, so that he could ascertain whether at those times there was a rise of tension. In the majority of the cases that had not been so. If there were, he put the case into the glaucoma group.

He had been puzzled by Mr. Sorsby's statement to-night that the cupping in this group was not the same as in glaucomatous cupping. By the method which he (the speaker) employed—of registering the shape of the disc-cup—he had tried, but in vain, to find a

distinction between the two types of cup. They both developed in the same way; the growth of the cup took place from normality to the complete thing, the progress through the stages being exactly the same in each case.

A few of these cases might go on for years, and, finally, develop a slight rise of pressure He had so far come across only one case in which the rise of pressure had been great. But when rise of pressure did occur, one was by no means justified in concluding that the case had been one of glaucoma from the beginning. That was shown very conclusively by a case of low tension which he had some years ago. Because one eye was nearly blind and the other was rapidly losing its field of vision, he performed a trephine operation in the better eye and brought the tension down well below the normal, and it stayed so. The eye which was blind and had not been operated upon developed a slight tension, up to 30 (Schiotz) after five years. But the operated eye continued to show a reduction in the field, i.e. the essential process which had been at work continued to be active, and the field decreased until the man was practically blind. There was just a minute field in the centre, and the tension was 12 (Schiotz). At present he had not made up his mind as to the causation. As to the fields, he found no difference; the earliest change in the field in glaucoma and in cavernous atrophy was the diminution of $\frac{1}{1000}$, and in most cases it was fairly concentric. The $\frac{3}{1000}$ field kept fairly well, but when it broke up it did so in a segmental way, as in glaucoma.

Mr. SORSBY (in reply to Miss Mann) said that skiagrams of the remainder of the skeleton in these cases had not revealed any other abnormality.

He had been glad to see the picture exhibited by Mr. Affleck Greeves, of a coloboma which had been produced by injury, but he could not offer any explanation of it.

He was least confident about his third group, and he welcomed criticism; yet he could not avoid the conclusion that it was a distinct group in itself. Arteriosclerosis was always present; in the first stage neither the cupping nor the field suggested glaucoma. Later on, it was possible there might be an extensive process which produced chronic glaucoma. He had seen ten instances, and in the early stage they were fairly characteristic. There was always a definite degree of arteriosclerosis, usually with some complication like occlusion of a vein or an artery, and a very characteristic cupping of the disc. He definitely felt that the cupping seen in the cases that he had shown was not the same cupping as was seen in glaucoma, and that his cases presented a typical picture, together with the arteriosclerosis.

He wished again to emphasize the field defect by the drawing [exhibited] of a case which he had seen for the first time on the previous day. The patient had optic atrophy and a pale disc, which was deeply cupped without any bending of the vessels, and there was very marked arteriosclerosis.

CASES

Tumour of Iris.—A. F. MACCALLAN, C.B.E., F.R.C.S.

The patient, a man aged 42, was shown at a Meeting of this Section on March 9, 1928.[1] At that time the tumour had been present for eleven years. He does not think that it is larger than it was six years ago.

Condition on examination.—Visual acuity, with small myopic correction, is full. The fundi are normal. A small tumour is situated on the lower part of the iris. The tissue of the decolourized tumefied area, in which the fibres of the iris are distinctly seen, seems to merge gradually into the normal pigmented iris tissue.

The scattered pigment on the surface is more marked than it was six years ago. In my opinion the tumour is slightly larger than when last seen.

Diagnosis.—Nævoid growth of iris with pigment.

Discussion.—Miss IDA MANN said that for six months she had been watching a woman, aged about 50, with an almost exactly similar condition of the iris, but not so large a tumour as that in the present case, and she did not feel sure as to its nature. During seven months of observation it did not appear to have altered, and she felt she was confirmed in her waiting policy by having seen Mr. MacCallan's case.

Mr. MACCALLAN (in reply) said that the pigment which was seen on the surface made him think it was more dangerous than at first it appeared to be. However, at the present time, no surgical intervention was contemplated.

[1] *Proceedings*, 1928, **xxi**, 1232 (Sect. Ophth., 48).

Mr. D. L. DAVIES said that a week ago he had seen a similar case, which he had seen six years previously. The tumour occupied one-fifth the circumference of the iris, in the upper quadrant. He had opened the anterior chamber and tried to remove a portion of the tumour: it was much too fibrous to permit of the removal of the whole; it was solid, and not obviously vascular. The microscopical report was that it consisted of embryological connective tissue. There were no signs of malignancy. When seen during the past week, the tumour looked exactly as it had done six years before. Unlike the condition in the present case, however, there was no granular pigmentation on the surface.

Mooren's Ulcer.—A. C. HUDSON, F.R.C.S. (President).

The patient is a man aged 71.

History.—Carbuncle of neck eleven years ago. Pernicious anæmia diagnosed five years ago; treated with liver and hydrochloric acid. Has taken liver powder since then fairly regularly.

Left eye became red in December 1932, and vision was misty. This condition had persisted until the time of the patient's first visit in May 1933. There was then a typical Mooren's ulcer of the upper part of the left cornea.

Satisfactory healing was not obtained until treatment with radium had been carried out at the Radium Institute by Dr. Roy Ward.

First treatment, August 28, 1933: Radium plaque containing 6·2 mgm. of radium element and having an active area of 1·25 cm. in diameter in actual contact with the lesion for one hour.

Second treatment, October 4, 1933, was the same as the first. There has been no sign of active ulceration for the last four months.

Section of Comparative Medicine

President—R. T. LEIPER, M.D., F.R.S.

[*November* 22, 1933]

DISCUSSION ON LOUPING-ILL

Mr. W. S. Gordon: *Comparative aspects of louping-ill in sheep and poliomyelitis of man.*—By louping-ill in sheep is currently understood a disease characterized by cerebellar ataxia and disorder of brain and spinal-cord functions, lasting from about a day in acute infections to some weeks in chronic cases. In the latter type, paralysis of one or more limbs is generally present. The mortality in definite clinical cases is high, but animals which recover do not usually develop another attack. The association of the disease with particular pastures is well established, and a large proportion of sheep brought from a locality in which louping-ill does not occur into a louping-ill district are liable to develop the disease.

The first conclusive contribution on the causation of this disease was made by Pool, Brownlee and Wilson [1] in 1930, and the earlier literature on louping-ill has already been reviewed by Pool [2], [3]. These authors recorded the successful transmission of louping-ill in series from sheep to sheep by intracerebral inoculation with material obtained from the central nervous system of affected animals. The pig also was shown to be susceptible. In continuation of the work of Pool, Brownlee and Wilson, investigations [4], [5], [6], [7], [8], [9] at the laboratories of the Animal Diseases Research Association established that (1) the infective agent is a filtrable virus which is communicable to mice as well as to sheep; (2) the pathological changes in the disease are essentially those of an encephalo-myelitis; (3) the virus may be present in an infected sheep without producing typical louping-ill, but blood drawn at an early stage of the febrile reaction, which is a prodromal symptom of this infection, contains the virus; (4) atypical manifestations may comprise merely a febrile reaction, or the sheep may die without lesions in the brain and spinal cord; (5) under natural conditions, louping-ill is tick-borne, the vector being *Ixodes ricinus* L., which is habitually present on louping-ill pastures; (6) recovery from infection, either naturally or experimentally produced, results in immunity; (7) the investigation of louping-ill has revealed the presence of another tick-borne infection of sheep. This disease, which has been named "tick-borne fever," is clinically, pathologically, immunologically and ætiologically distinguishable from louping-ill, but it probably aggravates the harmful effects of the latter.

That the causal organism of louping-ill is a filtrable virus is now generally accepted (Alston and Gibson [10], and Czarkowska-Gladney and Hurst [11]). Hurst [12] infected monkeys, and Findlay and Elton [13] transmitted the disease to field voles. We possess unpublished evidence that cattle also are susceptible, and may develop the disease naturally. Rivers and Schwentker [14] record that human beings who have come into close contact with the virus of louping-ill may develop in their serum neutralizing antibodies against the active agent, and illness suggestive of louping-ill infection is reported in three such individuals.

Our investigations into the pathogenesis of the disease in sheep and methods of prevention will soon be published in detail, but it may be stated here that there is a prodromal period in the naturally occurring disease, characterized by a diphasic fever. Virus can invariably be detected in the blood during the early part of the first febrile phase. The second febrile phase usually marks the commencement of symptoms indicating invasion of the central nervous system, and then virus is generally absent from the blood. Many natural cases of louping-ill, however, are abortive; in some of these, symptoms of central nervous system infection appear and pass off, whilst in others the only indication is dullness accompanying the characteristic febrile reaction. Abortive attacks can be diagnosed definitely by detection of virus in the blood during the first febrile phase, by intracerebral inoculation of mice with citrated blood. There is also evidence that subcutaneous inoculation with formalinized vaccine prepared from the brain and spinal cord of infected sheep, produces antibodies capable of neutralizing virus introduced into the general circulation, thus preventing the active agent from invading the brain and spinal cord. This vaccine does not immunize the central nervous system, but extensive field trials show that it affords a considerable degree of protection against the natural infection. These observations suggest that the primary multiplication of this so-called neurotropic virus occurs outside the brain and spinal cord.

Since this is a discussion in comparative medicine, it seems appropriate to direct attention to the somewhat similar syndrome of naturally occurring louping-ill in sheep and the course of poliomyelitis in man. Of course, it is not suggested that the two diseases are identical, but, since the pathogenesis and epidemiology of poliomyelitis are subjects of considerable controversy, the study of louping-ill in sheep may present some noteworthy features to those interested in poliomyelitis.

At the outset I would mention that, having no personal knowledge of poliomyelitis, I am greatly indebted to the Report by the International Committee on Poliomyelitis [15], organized by Jeremiah Millbank of New York City.

The medical pathologist, whose material is man, is drastically handicapped by the limited extent to which experiment on the natural material is open to him. He must take his problems as he finds them, and deny himself the help of almost all the preliminary simplifications which are the essence of the veterinary pathologist's advantage. When one's patient can be used as one's experimental animal, circuitous methods of investigation in determining the pathogenesis of a disease are not required. Thus, the investigation of louping-ill has been greatly facilitated by the fact that sheep, which are naturally susceptible to the disease, are also suitable experimental animals. Such facilities permit a study of the propagation of the infective agent in its natural host, and enable one to place greater reliance on the conclusions drawn regarding the natural route of infection and the epizootiology of the disease than can be placed on similar studies with an infective agent which has been adapted by artificial methods to an experimental animal. In the case of louping-ill, we have used the mouse mainly for determining whether virus is present in a given tissue. Fortunately, the pathogenesis of the disease could be studied in sheep. It was not necessary to make these studies on the mouse, and to argue from the analogous disease in that animal as to the nature of the infection in sheep.

Comparative aspects of the ætiology and symptomatology of louping-ill and poliomyelitis.—Each disease is caused by a filtrable neurotropic virus. Schwentker, Rivers and Finkelstein [16] showed that immunologically louping-ill and poliomyelitis are not closely related—incidentally, it may be noted that the poliomyelitis virus used in their experiments was the " mixed strain " virus highly adapted to the monkey. Now, it appears from the work of Burnet and Macnamara [17], Weyer [18] and others, that repeated passage of poliomyelitis virus through monkeys brings about an immunological change, and the recent work of Paul and Trask [19] shows that there is a qualitative immunological difference between a freshly isolated strain from a human source and a monkey-adapted strain. Accordingly, the question of immunological relationship between louping-ill virus and a freshly isolated " human " strain of poliomyelitis virus still remains open. The incubation period of naturally occurring louping-ill is usually between six and eighteen days, from the time of infection until the appearance of clinical symptoms. This corresponds with the incubation period of poliomyelitis infection. In the prodromal period of louping-ill infection there is usually a diphasic temperature reaction, and the second febrile phase is accompanied by the appearance of the first symptoms of nervous derangement, when these develop. This corresponds with the so-called dromedary type of prodromal symptom, described by Draper [20] for poliomyelitis. The virus of louping-ill has been detected in the blood of infected sheep concurrently with the initial rise in temperature, and in most instances a fall in temperature is followed by the disappearance of much or all virus from the blood. The virus of poliomyelitis has not been detected in human blood, but I am not aware that systematic daily examination of blood has been made during the prodromal stage. Arguing from the analogy of louping-ill, it is highly improbable that virus would be present in the blood when the symptoms of paralysis had developed. Flexner and Lewis [21] were able to show the presence of virus in monkey's blood if large quantities were drawn at the height of the disease. If the monkeys showed nervous symptoms at the time the blood was taken, these workers were probably fortunate in detecting virus. Leiner and von Wiesner [22] also reported success in 1 out of 5 tests with blood drawn from monkeys at different stages of the disease. Clark, Fraser and Amoss [23] detected virus in the blood of monkeys in 1 out of 10 instances; the important point about this positive result, however, being that blood was removed at a fairly early stage of infection, namely, at the beginning of paralysis on the seventh day following intracerebral inoculation. In poliomyelitis it may yet be found that, as in louping-ill, virus is invariably present in the blood during the early stage of the febrile reaction, and generally absent from the blood when paralysis has developed. In clinically obvious cases of poliomyelitis, paralysis of one or more limbs usually occurs. During epidemics the so-called abortive (Wickman type) and non-paralytic types of the disease have been recorded. The most convincing evidence of the occurrence of abortive cases has been furnished by Paul and Trask [24], who isolated poliomyelitis virus from the throats of two patients during a characteristic minor illness which was not followed by paralysis. In chronic cases of louping-ill, paralysis of one or more limbs usually develops, and on farms where the disease is prevalent sheep with various types of deformity are usually encountered. As already stated, the existence of abortive cases of louping-ill has been definitely established by the detection of virus in the blood during a febrile reaction, which was the only clinical manifestation of infection other than dullness and loss of condition. Such atypical infections are followed by immunity.

Comparative aspects of resistance and immunity.—It is stated that the low case incidence of epidemic poliomyelitis has generally been taken to indicate that many persons are exposed to the virus without developing the typical paralytic disease. This inference, however, is only an indirect one and is not based on direct experimental evidence. The analogous evidence in the case of louping-ill is direct,

since the specific virus has been detected in the blood of sheep during a minor illness accompanied by a febrile reaction which was not followed by paralysis. Further, in one of our experiments, 49 susceptible sheep were exposed to the risk of natural infection for two months; 53% of the animals died from all causes, and 60·9% of the survivors had acquired immunity to louping-ill. As in poliomyelitis, one attack of louping-ill usually confers immunity, and in both diseases neutralizing substances develop in the blood of infected individuals. The only reliable method of producing a typical case of louping-ill in sheep is by introducing the virus directly into the central nervous system. Subcutaneous or intravenous inoculation with virus is often followed by an abortive attack, or only a febrile reaction. In some instances, however, the typical disease, with involvement of the central nervous system, is produced. Intranasal insufflation with virus is an unreliable method of producing infection; admittedly, infection can be produced by this route, but, if it occurs under natural circumstances, it must be very rare. We have now had over 2,000 sheep under experiment without observing any precautions to prevent spread by contact, and we have no evidence to suggest that infection may spread by this means. The evidence on this point in regard to poliomyelitis in man is rather conflicting.

Active immunity.—In considering methods of prophylactic vaccination for the control of louping-ill, it was found that the central nervous system is a difficult tissue to immunize. Thus, formalinized vaccine inoculated subcutaneously does not protect sheep from virus injected into the brain, whereas it does protect against virus introduced subcutaneously. Subcutaneous injection of living virus, when followed by a febrile reaction in the inoculated animal, immunizes the central nervous system, but this method is attended by a risk of setting up the disease. Since the disease is transmitted under natural circumstances by a blood-sucking arachnid, and the primary multiplication of virus occurs in the blood, it was considered that the immunity afforded by the formalinized vaccine might be sufficient to prevent the natural infection. As already stated, although this vaccine does not produce immunity of the central nervous system, it is proving efficacious in the control of the natural disease.

Monkeys can be immunized against poliomyelitis by the subcutaneous inoculation of living virus. As in louping-ill, the method is attended by the danger of setting up the disease. To quote one example, Leiner and von Wiesner [22] inoculated four monkeys; one died of typical poliomyelitis after four injections; one developed the marantic type of the disease, and two died of an intercurrent infection. Success has not attended the efforts to produce immunity by dead virus vaccines. From the analogy of louping-ill, this is not surprising, since the immunized animals were tested by intracerebral inoculation.

Comparative aspects of the pathology.—The essential pathological changes in the two diseases are closely similar, and are mainly confined to the central nervous system, where inflammatory changes occur with destruction of nerve cells, mainly the anterior horn cells of the cord in poliomyelitis, and the Purkinje cells of the cerebellum in louping-ill. From the comparative point of view, it is essential to draw attention to the fact that although the sheep, mouse and pig are all susceptible to louping-ill, the nature of the reaction in the central nervous system of these animals varies. Thus, in the sheep, as the lesions suggest, cerebellar ataxia is the main symptom. In the mouse, the nerve cells of the cord are mainly affected, and there is usually paralysis of one or more limbs, whilst in the pig, which generally does not develop a fatal disease, the interstitial reaction predominates. Even in animals of the same species, the extent and location of lesions in the central nervous system may vary, and consequently the symptoms may not be typical.

Comparative aspects of the epizootiology of louping-ill and the epidemiology of poliomyelitis.—In forming an opinion on the epizootiology of louping-ill, it is probably well to bear in mind the insulatory mechanism which guards the central nervous system from injurious substances of hæmatogenous origin. Wilfred Trotter [25] gives a very clear conception of this mechanism. After reviewing the evidence, he states:—

"We have a group of well-defined facts established by countless observations and capable of confirmation any time. They bring evidence from different parts of the nervous system, disclosing, even to superficial consideration, a clear common tendency. The conclusion to which all point is that breaches of normal coverings of the nervous tissues allowing contact between the latter and other tissues of the body, result of necessity in energetic local reactions. The obvious function of such reactive processes is to re-establish the normal discontinuity between neural and somatic tissues, and to break the contact that has caused the disturbance."

McIntosh and Fildes [26] found that after intravenous injection of salvarsan and neosalvarsan in man and animals, no arsenic could be found in the brain, although its presence could be detected in tissues outside the central nervous system. This phenomenon is not due to a lack of affinity between the brain and the drugs, but to an inability on the part of the drugs to penetrate into the substance of the brain. After subcutaneous inoculation of massive doses of potent antitoxin into sheep, we have found that although the antitoxin can be detected in the blood, its presence cannot be detected in the cerebrospinal fluid. Whilst it cannot be argued that these substances are comparable to a living virus, the evidence suggests that injurious materials present in the blood have very definite barriers to overcome in gaining access to the central nervous system. It would appear that the epizootiology of louping-ill is closely linked with this fact, and the perpetuation of the disease in enzootic form is dependent on a high case incidence of the so-called abortive form, with a relatively low incidence of clinical cases; that is, cases in which virus has invaded the central nervous system. This aspect of the problem may also have some bearing on the explanation of the epizootiology and epidemiology of other diseases caused by so-called neurotropic viruses. It is generally recognized that a large proportion of old sheep on a "diseased" farm are immune to looping-ill, although they have no history of a clinical attack of the disease. Even in a group of yearling sheep received from diseased farms, Pool, Brownlee and Wilson found that 20% were immune, and we have found that after exposing susceptible sheep to the risk of natural infection for two months, as many as 60·9% of the survivors were immune.

Endemic poliomyelitis has its greatest incidence in children up to five years of age. There is an unexplained seasonal incidence, and it is generally regarded as a summer disease. Enzootic louping-ill is generally confined to lambs and yearling sheep; its incidence is also seasonal, occurring in the spring, and, to a smaller extent, in the autumn. The seasonal incidence of louping-ill corresponds with the season of maximum activity of ticks, which are the vectors of the disease. When an epizootic of louping-ill occurs in a sheep stock in which the disease has not been previously recognized, animals of all ages are liable to become affected. Similarly, epidemics of poliomyelitis in "virgin soil" have the same tendency. In the International Committee's Report, three "virgin soil" outbreaks are described; one upon the island of Guam in 1899, reported by Grunwell; one upon the island of Nauru in 1910, reported by Müller; and one in New Guinea in 1929, reported by Macnamara. In each outbreak there was a high mortality, mainly in young adults. An extraordinary feature common to each outbreak was the apparent immunity enjoyed by the children. This is a peculiar phenomenon, and might suggest that

the incidence of subclinical cases in children greatly exceeds frank cases, with definite involvement of the central nervous system, whereas this may not be the case with non-immune young adults.

Among the many opinions on the epidemiology of poliomyelitis, the one expressed by Lavinder, Freeman and Frost [27] is of particular interest. They state that:—

> "While the incidence among a population affected by poliomyelitis, even in its severest epidemic form, is usually not high, yet this disease possesses not infrequently the power to spread widely—in fact, to become pandemic in a country. It has been suggested that an epidemic of infectious disease may be viewed as the resultant of two excursions, a vertical one representing the heaping-up of cases in any locality, as usually shown plotted on a chart, and a lateral one representing the extent of territory covered—the geographic distribution. Epidemic diseases not infrequently show decided variation in these two movements. Certain of them like dengue, for example, show a most striking vertical movement along with a very limited lateral movement. Poliomyelitis has exhibited a significant power of lateral movement, and, up to the present time, in much greater degree than its power of vertical excursion."

This "creeping tendency," as Dale [28] calls it, suggests a limiting factor of host resistance, a sparse but widely spread population at risk, and a widespread virus. This opinion on the epidemiology is compatible with the view that poliomyelitis may be a systemic infection with the specific virus which, under favourable conditions successfully invades the central nervous system and is responsible for the symptom-complex of poliomyelitis. Such a definite view would materially assist in solving many of the baffling problems in the epidemiology of poliomyelitis. In view of the modern trend of opinion (Walshe, Annual Meeting of the British Medical Association, 1933) that poliomyelitis is probably, from the outset and exclusively, an infection of the nervous system, it may be of comparative interest to draw attention to the fact that in an analogous disease of sheep—louping-ill—there is a high infection incidence of the young population, a large proportion of the cases being sub-clinical infections which can only be diagnosed by detection of virus in the blood, and a small proportion of frank cases with symptoms indicative of central nervous system infection. Thus in the perpetuation and spread of this disease, systemic infections probably have a more important rôle than actual clinical cases.

Summary.—Louping-ill, an encephalomyelitis of sheep, is caused by a filtrable virus possessing neurotropic characters. Under natural conditions of infection, the disease is tick-borne, the vector being *Ixodes ricinus* L. At first it would seem a curious anomaly that a blood-sucking arachnid has the rôle of transmitting a neurotropic virus, but the apparent anomaly is explained by the fact that multiplication of this so-called neurotropic virus occurs primarily in the blood. Invasion of the central nervous system by the virus occurs at a late stage in the infection, and is responsible for the characteristic symptoms of the disease. In the naturally occurring disease, invasion of the central nervous system is not a constant feature. Cases occur in which virus does not gain access to the central nervous system. Such abortive types of the disease can be diagnosed by the detection of virus in blood drawn at an early stage of the febrile reaction which accompanies the infection. It seems highly probable that the incidence of abortive types of the disease greatly exceeds the number of frank cases with central nervous system involvement.

From a comparative point of view the study of louping-ill in sheep would suggest that in the early stage of poliomyelitis in man, before obvious clinical symptoms have developed, the specific virus may be present in the blood. If such early blood infection were demonstrated, present views regarding the nature of poliomyelitis infection, and its prevention and treatment, would require revision.

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Mr. W. A. Pool: "Louping-ill" has, hitherto, only been regarded as of interest to a limited community—sheep farmers and those associated with them, in a restricted part of a small country. During the last year or two, however, considerable interest has been aroused in the subject, for various reasons, notably the opportunity of studying a new virus which is easily obtained, and easily and cheaply maintained in the laboratory, one that has properties somewhat comparable to those of an important human virus, and is itself capable of infecting man.

Nomenclature.—The nomenclature of louping-ill has not raised the general scientific standard of virus disease nomenclature, but the name perhaps has the advantage of being descriptive, although, in my experience, it emphasizes a part of the syndrome that is not striking to the observer who is shown declared cases. It rather emphasizes the extraordinary observational powers of the shepherd and flockmaster as indicating a prodromal stage—a stage of hyperæsthesia, which may be of very brief duration, and in many cases easily overlooked—representing a phase of the syndrome which appears to them to be outstanding, the paralytic symptoms and deaths being, from their point of view, merely fairly common sequelæ.

The term "louping-ill" is, however, only used on the borders of England and Scotland. In affected parts of the Western Highlands the disease is called "trembling."

This brings up another point in nomenclature. "Scrapie," a sheep disease of unknown ætiology, of very restricted distribution, and devoid of any resemblance to "louping-ill," is known in continental literature as "La tremblante" or "Traberkrankheit." It is natural for continental writers to translate "trembling" into "la tremblante," and then opportunities for misunderstanding are opened up. This actually occurred recently, a French writer, Lépine, having used the term "la tremblante" in connexion with work on "louping-ill" virus sent to him by me.

The incidence of louping-ill.—As far as I know louping-ill is only known in certain areas of the border counties of England and Scotland, and in the Western Highlands. A word of warning is necessary here. The Board of Agriculture, Braxy and Louping-ill Committee of 1900, published a map showing a number of affected areas in England and Scotland. The Committee sent a questionnaire to

sheep farmers, and apparently accepted the statements received in reply. The map published by the Committee, and said to show the distribution, should therefore be regarded with suspicion.

The type of farm is always rough hill grazing, and it is on such land that ticks are found. There is still much to learn as to the conditions determining the presence or absence of louping-ill on farms in the affected areas. To study this question I obtained a complete map of the county of Selkirk, showing all the farm boundaries, and commenced to make a detailed survey of all the land in the county, and to mark that affected and the various conditions that appeared to be of importance. "Affected" and "clean" farms are often fairly close together, a point which is referred to in the third report of the Committee of the Highland and Agricultural Society (1884). To take one district as an example—the Ettrick valley in the county of Selkirk. The farmer, from whose sheep the virus was originally isolated in 1929, has a number of sheep farms all within a radius of about twelve miles, and in more or less the same type of hilly country. At least two of his farms which, roughly, appear to be fairly similar to affected ones, are definitely "clean," and he cannot safely bring sheep from a "clean" farm to an affected one during the season when ticks are prevalent. It is often said that the farms at the top of the watershed tend to be "clean."

Unfortunately, for certain reasons it was not possible to proceed with this survey.

Susceptible species of domesticated animals.—The disease primarily affects sheep. There is plenty of evidence that, on some farms, cattle contract the disease if grazed on infected areas, but the danger to cattle is apparently considered by farmers to be greater in some parts of affected country than in others. In some parts there is a history that pigs on affected land may contract the disease. Most shepherds keep a pig or two for their own use and, on louping-ill farms, are often careful that the pigs do not leave the sties. On the farm from which the virus was first isolated, however, there was no history of infection in pigs. I have never heard of louping-ill in a horse, although horses are exposed on affected land. The susceptibilty of wild animals and birds is worth attention.

Seasonal incidence.—This is very marked: the important season in all louping-ill areas is the early spring, varying to some extent from year to year, but occurring roughly from the middle of March to the middle of May. In some parts, in my experience in the Western Highlands, there is a marked, but less important, incidence rise in the autumn. In other areas, however, autumnal incidence is not mentioned.

Early investigations.—Now that the cause of the disease is known, it may appear unnecessary to waste time over the earlier work on the subject. The disease, however, has not yet been controlled or eradicated, and much of the earlier work may be of value when interpreted in the light of modern knowledge.

Some of the earlier investigators were hampered by lack of knowledge of particular aspects of the problem. For example, in the work carried out at the end of the last century, the ignorance of the writers as to the life histories and habits of the ticks concerned resulted in faulty experimentation. Ignorance of bacteriology or misapplication of knowledge, which were not always justifiable, were responsible for most of the errors—notably in the work of Klein (1893), of Meek and Greig Smith (1896 and 1897)—of those responsible for the report of the committee appointed by the Board of Agriculture (1906) and of McGowan (1915). M'Fadyean (1894 and 1900) pointed out the errors of previous authors who had worked on louping-ill and his statements are still sound. There is a curious omission on the part of some of the later authors to give attention to M'Fadyean's articles.

There can be little doubt that Stockman produced the disease in some of his

inoculation experiments, but the results were so irregular that it has always been difficult to assess the general importance of his work. In most of his experiments in sheep the reactions to inoculation were limited to a rise in temperature, in many cases only to 105° F. The number of instances in which a syndrome comparable to that of louping-ill was produced was small: and, in some of the experiments, the inoculum was contaminated. In such circumstances the production of paralytic symptoms in an odd case could not be given weight. It is to be presumed that "tick-borne fever" caused at least some of the temperature reactions obtained by Stockman.

The history of the investigations leading to the isolation of the virus is perhaps worth discussion.

By 1928 much information as to the disease had been accumulated, but intensive work on the subject was not possible. As an odd experiment, there was an opportunity, in 1928, to feed and inoculate young pigs with material from louping-ill cases. The pigs fed on various tissues remained healthy. One pig, however, which was inoculated subcutaneously with a suspension prepared from the spinal cord of a natural case, and two days later inoculated subcutaneously with similar material from another case, developed a febrile reaction after an incubation period of a few days. Twelve days after the first inoculation it was acutely ill and trembling violently; quite early in the illness there was paralysis of the muscles supporting the head so that the nose could not be lifted off the ground. The animal recovered from the general symptoms, but the paralysis was still very marked, and, in the course of a year's observation, the use of the muscles was gradually and partially restored. At the time this was merely regarded as an interesting result, as similar inoculations in sheep had so often failed to produce such a syndrome. There was no opportunity, however, to repeat the experiment until the following year.

At the beginning of the 1929 louping-ill season, it was possible to deal intensively with the work.

Inoculation experiments in pigs and sheep by the intracerebral route with inoculum freshly prepared from the central nervous system gave positive results. The reaction in pigs, however, bore a closer resemblance to the typical louping-ill syndrome than did those in sheep: in pigs, paralytic symptoms and tremors were striking, but in sheep the disease tended to run a peracute course, and this might have been attributed to the operative procedures.

Owing to the numerous records, in earlier published and unpublished work, of failure with sheep, passage in pigs was relied on at first and this soon led to a disconcerting check, as the virus could not be passaged through more than one generation in pigs. It was soon obvious, however, that virus passaged through pigs was infective to sheep, but not to pigs, and that it could be maintained in series in sheep or in sheep to pig. Thereafter, pig inoculations were omitted and sheep were used exclusively for the main experiments. It was then relatively easy to work out the preliminary stages of the study of the virus—its distribution in the body, the paths of infection, the viability, the dilutions in which virulent material would infect, etc.

Why was the virus not found by the earlier investigators?—This point is worth attention as something may be learnt from it which may apply to similar investigations in the future.

The virus was missed by the earlier investigators because they did not design and follow a suitable plan of sufficient magnitude. The reasons for their failure may be classified thus:—

(*a*) Failure to investigate systematically and thoroughly potentially infective tissues; (*b*) failure to allow for a fairly big margin of regular response in the test animals—in other words, to use systematically sufficient test animals in each

experiment; (*c*) failure to work systematically and thoroughly through the potential paths of infection. Through one or other of these causes, some investigators no doubt just failed to discern the truth, while others were probably unfortunate in meeting with atypical response on the part of some of the few animals used in the experiment. Moreover, the failure in these circumstances misled others who followed them.

Tick eradication.—Whether or not tick eradication in affected areas is economically worth while has still to be settled. It would be a great advantage to remove ticks, but that would not eliminate all the serious sheep disease from these farms. It would presumably improve the value of the farms, but it is difficult to assess the extent of such gain.

Miscellaneous observations.—One of our earliest experiments was to ascertain if contact infection occurred in sheep, but the results were negative. The only evidence of contact infection in experimental conditions is that of Alston and Gibson (1931), who claimed that it occurred in mice and now there are the recently reported infections in human beings. I have carried out some relatively small-scale experiments with mice infected by intracerebral inoculation, which were placed in contact with healthy mice, but never saw an instance of contact infection. Nor have I heard of a human being contracting louping-ill on affected farms. When I first heard of human infections, I wrote to a well-known landowner in the Western Highlands, who is interested in the general question of louping-ill and has infected farms, to ask his experience of human infection. After making inquiries in his neighbourhood, he informs me that he cannot trace any suspicion of such an occurrence. It is possible that cases do occur, but are wrongly diagnosed, or perhaps looked upon as cases of influenza.

The virus which has infected human beings has, of course, presumably become very artificial from passage in mice. There is great variation in the reaction of susceptible species to louping-ill, ranging from that exhibited in the pig to that in the sheep and in the mouse, these reactions being comparable to the effect of the virus on the nervous system. Transfer in animals such as mice, which show such a different reaction from that of sheep, must profoundly modifiy the virus. Hence it is possible that virus artificially passaged in mice is more dangerous to man than field virus. Those of us who worked in 1929 must have come in contact with heavy infection in sheep and pigs, but all appear to have remained in perfect health.

This brings up the question of the policy to be adopted in working with such a virus. Data obtained from a study of a highly modified virus may yield misleading results. Perhaps it would not be unfair to suggest that work on poliomyelitis virus has often suffered from the fact that it has been carried out with virus which has become artificial owing to years of passage in laboratories. It is easy to obtain field louping-ill virus in the spring and autumn and it can easily be maintained *in vitro*, so there should be little difficulty in using virus that has undergone a minimum of modification.

Finally, louping-ill virus offers to workers in this country a wonderful field of study, as it is a unique example of an easily available virus disease in which an invertebrate vector is considered to be involved.

Apart from the general observation of circumstances in which transmission is effected, a detailed study of the virus in the tick yields a great opportunity for important fundamental research.

Mr. I. A. Galloway: A study of the filtrability of the virus of louping-ill through graded collodion membranes has been made by Elford and Galloway (1933). Previous investigators, who had almost invariably employed broth as a medium

of suspension, found that the virus consistently passed the more permeable grades of laboratory filter candles. We found that a stock filtrate through a permeable collodion membrane of A.P.D. 0·5 μ to 0·8 μ was of high virus potency. The limiting infective dilution of such stock filtrates was invariably at least 1 : 100,000. A collodion membrane of an A.P.D. 40 mμ always completely retained the virus under the best possible conditions for filtration. The size of the virus particles is therefore estimated to be 15 to 20 mμ. The virus is second only to that of foot-and-mouth disease in order of smallness among the viruses so far examined. The filtration end-point was checked by inoculation of both mice and sheep. Another point of interest is that the virus proved to have retained its infectivity for sheep after forty passages in mice over a period of 687 days.

Buffer solutions, containing inorganic salts, such as phosphate and boric acid-potassium chloride mixtures, were found to be injurious to the virus (Elford and Galloway, 1933). Schwentker, Rivers and Finkelstein (1933) also reported that Locke's solution has a similar toxic effect on the virus. The pH of virus suspensions in broth must therefore be adjusted by addition of 0·1 N hydrochloric acid and 0·1 N sodium hydroxide. The virus (broth filtrates) dies off rapidly at room temperature, a 90% drop in infectivity occurring in twenty-four hours at pH 7·6, and even greater deterioration at a more acid or alkaline pH.

The general impression conveyed by the results when the virus was kept in the cold (4° C.) was that it survives best in slightly alkaline medium, pH 7·5 to 8·5. Systems at these hydrogen-ion concentrations, after seventy days' storage in the cold, were found to be still infective.

Our results (Elford and Galloway, 1933), and those of Webster and Fite (1933) have shown quite definitely that mice can be regularly infected by the intranasal instillation of virus. In our experiments mice from nine different stocks were found to be equally susceptible to infection by this route. It may be recalled that Hurst (1931), Findlay (1932), and Schwentker, Rivers and Finkelstein (1933) succeeded in infecting monkeys (*M. rhesus*) by the intracerebral inoculation of virus. The results of recent experiments, made in collaboration with Dr. J. R. Perdrau and to be published later, have shown that monkeys can also be infected by the intranasal instillation of virus. A progressive ataxia of cerebellar type was the dominant clinical feature, as in the case of monkeys infected by the intracerebral route. Proof of infection was obtained by recovery of the virus by mouse passage from the nervous tissue of monkeys developing fatal symptoms, by cell counts on the cerebrospinal fluid during the course of the disease, there being a mononuclear cytosis, by examination of the sera of recovered monkeys for neutralizing antibodies, and by histological examination of the nervous tissues. Sections stained by Bielschowsky's silver impregnation method showed that, in spite of the disappearance of the Purkinje cells, the basket network was preserved (*cf.* "parenchymatous cortical cerebellar atrophy in the human being") (Parker and Kernohan, 1933).

Rivers and Schwentker (1933) recently reported that four individuals, who had come in close contact with the virus showed signs of a non-fatal illness "which seemed to be influenza" and which in three instances was followed by encephalitis. The authors also conclude, from their results of a comparative examination of the sera of these patients and of various other human sera, that individuals who come in close contact with the virus of louping-ill may develop in their sera neutralizing antibodies against the virus.

We have examined a number of human, monkey, and sheep sera and our results will be published later. Only those sera from monkeys or sheep previously infected with the virus have shown virus-neutralizing properties, and a general consideration of these results, along with those we obtained from the examination of human sera, strongly suggests, as Rivers and Schwentker (1933) have indicated, that man can be

infected with the virus of louping-ill with an accompanying development of antibodies in the serum.

We have not found that sera from humans or monkeys recovered from poliomyelitis are capable of neutralizing the virus of louping-ill (cf. Schwentker, Rivers and Finkelstein, 1933).

Finally, I wish to mention some preliminary experiments made with Dr. F. M. Burnet, the results of which indicate that the virus of louping-ill can be propagated in the developing chick embryo. It has been found on testing eggs inoculated with the virus, that the virus is present not only in the chorio-allantoic membrane, but also in the tissues—e.g. the brain—of the embryo in high concentration.

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Section of Dermatology

President—HENRY MACCORMAC, C.B.E., M.D.

[*December* 21, 1933, *continued*]

Necrobiosis Lipoidica Diabeticorum (Urbach-Oppenheim).—ROBERT KLABER, M.D.

This woman, now aged 36, was shown by Dr. H. W. Gordon at a meeting of this Section in May 1932,[1] as a case for diagnosis. (? Pseudo-xanthoma elasticum.) I am showing her to-day through the courtesy of Dr. Roxburgh.

She has been a telephone-operator for twenty years, and has always enjoyed good health. She states that she has always drunk and passed plenty of water, but that there has been no recent increase of intake or output. There have been no other diabetic symptoms, and her weight has remained constant.

Five years ago, preceded by irritation, a nodule appeared on the right instep. A few months later a similar nodule appeared on the front of the left ankle. At long intervals since, further nodules have appeared on the front and back of the legs (see Plate), on the right knee and the left elbow. The appearance of each fresh lesion is preceded by irritation, and the development of each has been observed to pass at varying rates through several phases.

(1) Initially, a small fawn-coloured infiltrated papule.

(2) This increases in size and becomes violaceous in colour.

(3) A raised, firm, yellow plaque develops in the centre. At this stage the lesion strongly suggests an "inflamed" xanthoma.

(4) The firm yellow plaque softens, and sometimes ulcerates, leading to a scanty thick discharge. This ulceration may be omitted.

(5) Ultimately the lesions extend further in area, while flattening out. This extension ceases after a few weeks. At the final stage there is some yellowish white central atrophy, surrounded by an irregular scaly red or violaceous area of infiltration, with some marginal pigmentation.

These lesions all persist, and have not been influenced by two full pastille doses of X-rays. The appearance of untreated lesions does not differ appreciably from those so treated.

Bacteriological investigation has been negative.

Wassermann, Sigma and Mantoux reactions negative.

Sections obtained from a biopsy two years ago showed with appropriate staining, a marked degree of fatty infiltration, elastic dystrophy, and a surrounding foam-cell and histiocytic infiltration.

Apart from their unusual clinical behaviour, since none of the fat showed double refraction, it was thought that the lesions could not be xanthomata.

Since the case was previously shown, several new lesions have appeared and passed through the phases already described. Their observation over many months has at last made it clear that the condition is that recently described by Urbach as "necrobiosis lipoidica diabeticorum." Balbi has only this year described the occurrence of such ulceration as is present in this case.

I do not think anyone who reads Urbach's or Balbi's original descriptions will have any doubt as to the essential identity of this case with the cases previously described. (The first case was shown by Oppenheim to the Viennese Dermatological

[1] *Proceedings*, 1932, xxv, 1551 (Sect. Derm. 83).

Society in 1929-30, as a "peculiar disseminate degeneration of the connective tissue in a diabetic.")

This woman's case differs, however, in several respects. Unlike the other three patients who were known diabetics, this patient has had no symptoms whatsover of this condition. Nevertheless, her fasting blood-sugar shows 300 mgm.% and her blood-sugar curve, kindly estimated by Dr. G. A. Harrison, is "typically diabetic." Blood-cholesterol has been 166 mgm.% (in October) and 195 mgm.% (in December), having apparently risen while she has been on a low-fat diet, but is still within normal limits (Dr. Harrison).

The most important deviation, however, from the cases hitherto described, has been the occurrence of what one might call the "xanthoma phase" in the lesions, suggesting that these two conditions are not so distinct as previous case descriptions would suggest. This is borne out by the examination of further fresh biopsy material.

Urbach and Balbi both report that their sections contain no doubly refracting crystals of cholesterol. A section from this case though showing only a few such crystals, confined to the centre of the fatty foci, does not contain a much smaller proportion than that seen in some xanthomata.

The modern treatment of diabetes with a low-fat and relatively high-carbohydrate diet, plus insulin, has been recommended, and will be instituted in this case.

Further investigations are being carried out, with regard to the marked vascular changes held by Balbi to be primarily responsible for this condition. I can only say at present that vascular changes particularly affecting the intima are present in some of my sections, but I have not yet seen anything approaching the degree described by him.

The clinical examination of the lungs, retinæ, and blood-pressure have not yielded any important results, nor have skiagrams of the limbs (for calcification) or the microscopic examination of the urine.

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Discussion.—Dr. I. MUENDE said that though the crystals which Dr. Klaber found might be cholesterin granules, as he suggested, they need not be that substance, as they did not show the characteristic colour. They were usually more yellowish, and in this case they were pinkish in non-polarized light. It might be that in this case one was dealing with some lipoid substance, and not necessarily cholesterin.

Dr. KLABER (in reply) said that he had very carefully compared the very few doubly refracting crystals present with those from a section of a diabetic xanthoma, under the same microscope, and he had been unable to find any difference between them. He agreed that the crystals were lightly coloured, but this depended on the strength and age of the staining. There was no certainty that the crystals in this case were cholesterin—there was no certainty that such crystals seen in any xanthoma were cholesterin—but these were strictly comparable to those seen in some xanthomata, though constituting only a small proportion of the total lipoid.

Postscript 28.3.34.—The patient has now been for two months under the care of Dr. George Graham and has been taking 10 units of insulin with 100 grams of carbohydrate per diem. The urine soon became sugar free, and the blood-sugar has fallen to 120-140 milligrams per cent. The appearance of the skin lesions is so far unchanged, though they are less infiltrated. No new lesions have appeared.

[R. K.]

John Bale Sons & Danielsson, Ltd London.

KLABER: Necrobiosis Lipoidica Diabeticorum (Urbach-Oppenheim).

UNIV. OF MICH.

[*January* 18, 1934]

Lupus Vulgaris.—ARTHUR BURROWS, M.D. (for W. J. O'DONOVAN, M.D.).

W. P., male, aged 1 year, admitted to the London Hospital, December 4, 1933.

History.—A small spot was noticed on the left cheek at the age of 3 months. Later on glands became enlarged in front of left ear. The lesion on the face increased in size nearly up to the time of admission to hospital.

In June 1933 the glands were incised and cheesy matter was evacuated. The mass has discharged intermittently until recently.

In September 1933 the child's father was invalided out of the Navy and entered a sanatorium.

Lupus vulgaris.

Condition on admission.—Dry reddish, slightly ulcerated area on left cheek, with a few apple-jelly-like nodules, size about 2 cm. in diam. The pre-auricular glands were enlarged, firm and purple. No other glands were palpable.

The material in the gland did not permit of bacteriological examination, but the reaction to a Mantoux test was positive.

No local treatment has been applied to the cheek lesion in order to preserve it as much as possible for this meeting. Daily general light baths have been given, however, and the cheek lesion has diminished in size and prominence.

Two main points of interest are involved in this case:—

In the first place the youth of the patient is notable. We saw the child first at the age of 10 months, and the face lesion dates from seven months earlier. One other case of lupus in a child, aged 10 months, is recorded at the London Hospital Light Department.

The other point is as follows. It is customary in most diseases, such as syphilis, to look for a primary lesion when glands are enlarged. In tuberculosis, beyond more or less vague ideas of infection arising from the tonsils, chest, and gastro-intestinal tract, enlarged tuberculous glands are usually accepted as a separate clinical entity. In this case we have a definite primary tuberculous lesion of the skin leading to the formation of secondary glands, and it is possible, as other cases have been observed elsewhere, that skin infection may more often be the cause of chronic tuberculous glands than is usually thought to be the case.

Discussion.—Dr. H. C. SEMON said that this case was of great interest: it was the first of the kind he had seen, though he had read of three cases which were reported in Germany last year. One was that of a girl who also developed a primary typical lupus patch on one cheek. Her fiancé—a tuberculous sailor—had left on a sea voyage on a date, somewhere about a month, prior to the appearance of the nodule. This enabled the incubation period of the infection to be approximately determined. Tubercle bacilli were found in the nodule which resembled ordinary lupus vulgaris and, as in this case, secondary tuberculous glands developed in due course.

Dr. HUGH GORDON said that a year ago he had published a case of "Primary tuberculous chancre," in a child, aged 5 years. Later on, the submaxillary glands became acutely swollen, and tubercle bacilli were extracted from them in large quantities. There was also transitory erythema nodosum.

Dr. H. W. BARBER said that Lehmann had published ten cases of infants in whom primary tuberculous chancres had developed on the penis after circumcision by a phthisical rabbi.

Telangiectasia (? Osler-Rendu-Weber Familial Telangiectases) in Association with Raynaud's Disease. — J. E. M. WIGLEY, M.B., and GORDON HEGGS, M.D.

Name.—Mrs. F. C., aged 52.

History.—About ten years ago patient noticed some small, red spots on the face and lips. Approximately seven years ago similar spots appeared under the finger nails. At about this time she began to have attacks of whiteness, followed by blueness, of the fingers and toes. There has been no malaise or illness of any kind, including epistaxis, bleeding of the conjunctivæ, hæmatemesis, or hæmaturia.

Family history.—One son has periodic attacks of epistaxis. One brother has melæna. The mother has hæmaturia.

Condition on examination.—The patient appears to be a well-developed and well-preserved woman. She has been seen during an attack of Raynaud's disease of the hands and feet. There is a tissue-paper scar one one shin. The blood-pressure is 190/100. The spleen is not palpable. There are no varicose veins.

Skin and mucous membranes.—There are numerous small telangiectases on the malar region of the face and on the mucous membranes of the lips and under the finger nails. There are no lesions on the body or on the lower limbs.

Laboratory findings.—Blood: Wassermann reaction negative.

Sedimentation rate of the blood = 3 millimetres for the first hour (normal).

Bleeding time and coagulation time, normal.

Blood-count.—Blood-platelets 272,800 c.mm.; R.B.C. 5,200,000; Hb. 102%; C.I. 0·98; W.B.C. 6,100. *Differential*: Polys. 57%; eosinos. 1%; large hyals. 5%; lymphos. 36%.

Histology (Dr. I. Muende).—Section shows simple telangiectasia with some intracellular hæmorrhage.

The epidermis shows no material change. The superficial blood-capillaries of the dermis are greatly dilated, and in spaces the walls are broken, with resulting hæmorrhage into the corium. Here and there one can see the presence of pigment due to the breakdown of hæmoglobin.

This case apparently comes into the group of familial telangiectasia, which has been described by Osler, Parkes Weber and others, but we are not aware of its having been described as occurring in association with Raynaud's disease.

Discussion.—Dr. PARKES WEBER said he thought this was a very good example of telangiectasia of the skin and mucous membranes, of the Osler type. He was not sure that an association with Raynaud's disease had ever been described before. He would prefer to use the phrase "recurrent Raynaud's syndrome (symptoms)" in connexion with the present case, as these attacks might prove to be the first indication of sclerodactylia. Typical sclerodactylia often commenced with recurrent attacks of Raynaud's syndrome.

Dr. H. W. BARBER said he considered that an association of telangiectatic lesions of this type with Raynaud's disease was absolutely characteristic, so much so, indeed, that one could sometimes diagnose Raynaud's disease from the patient's facies; the lips were usually bluish, and dilated telangiectatic lesions were scattered over the face and on the mucous membranes of the lips, palate, and inside the cheeks. He had two patients with this syndrome whom he had had under observation for years; one of them had also commencing sclerodactylia, and both had calcareous nodules on the elbows and along the backs of the ulnæ.

Dr. PARKES WEBER said he was most interested in Dr. Barber's remarks; it was the first time he (the speaker) had heard the suggestion now made by Dr. Barber. He was familiar with cases of sclerodactylia, very likely accompanied by Raynaud's symptoms, which sometimes showed marked telangiectases, especially of the face; but it had never occurred to him that those cases were a combination of the Osler type of telangiectasia of the skin and mucous membrane with either Raynaud's syndrome or sclerodactylia.

Lupus Erythematosus. Case for Diagnosis.—J. E. M. WIGLEY, M.B.

D. V. R., a girl aged 7, poorly nourished but apparently healthy.

May 1933.—An irregularly reddened and scaling area appeared around the right eye and spreading on to the cheek and nose. (? Atrophy). Slight ectropion with epiphora. Similar scaling patch about the size of a shilling on right shoulder. No weeping. No itching. Present about a year.

October 1933.—Lesion noticed at left outer canthus.

November 1933.—Scaling area with reticular erythema around the right eye and spreading on to the nose; similar lesion at the left outer canthus, and on the anterior nares. Slight ectropion showing some atrophy.

Histological report (Dr. I. Muende).—June 1933: *Biopsy*—The section shows some acanthosis, hypertrophy of the stratum granulosum, and hyperkeratosis with a slight amount of parakeratosis.

January 1934.—There is a considerable acanthosis with widening of the rete pegs. For the greater part of the section there is proliferation of the stratum granulosum, together with hyperkeratosis, but at one end the stratum granulosum is absent, and the superficial layers, parakeratotic. Beneath the parakeratotic layers the rete malphigi shows definite intercellular œdema. In the corium there is very slight dilatation of the blood-vessels, but more marked widening of the lymphatic spaces. The small round-celled infiltration is almost entirely confined to the perivascular regions. The histological appearances would correspond with erythema migrans (Lipschutz).

The Wassermann reaction is negative.

I suggest that this is a very unusual distribution, and at an unusual age, for a case of lupus erythematosus.

Mycosis Fungoides.—J. E. M. WIGLEY, M.B.

Mrs. A. C., aged 65.

Previous history.—No abnormality of the skin until eight years ago when a red, scaly patch appeared on the areola of the right breast. Three or four years later similar patches appeared on the legs, spreading downwards from the thighs, and up the anterior and posterior aspects of the trunk to the neck, and later to the face. Six months ago patches appeared on both arms; one, on the inner side of the left arm grew larger and became ulcerated and fungating. Three months ago it suggested epithelioma, and there was one hard gland in the left axilla. Some pruritus.

Distribution of rash.—Face: Infiltrated scaling plaques on forehead, above left eyebrow; on bridge of nose and left upper eyelid, both malar prominences, tip of nose, upper lip and chin. Arm and legs (chiefly extensor aspects): Numerous infiltrated and scaly plaques. Trunk: More extensive, though less infiltrated, plaques on lateral aspects rather than on middle. On the inner aspect of the left upper arm is a long ulcerated area with indurated edges.

Histological examination of two sections (Dr. I. Muende).—The epidermis shows considerable acanthosis with narrowed and occasional forked prolongations of the rete pegs. There is considerable intercellular œdema, which, in the parakeratotic zones is very accentuated, giving rise at times to large vesicles in the rete. In addition one can see the migration of numerous lymphoid and polymorphonuclear cells between the individual epithelial cells. There is no excessive pigmentation of the epidermis. The papillæ are very dilated and œdematous, and are seen to contain lymphoid cells both small and large, eosinophils, and also some large endothelial cells. The greater part of the corium is infiltrated with closely packed endothelial cells, and cells which have the appearance of large lymphoblasts, the nuclei of which present numerous mitotic figures. Where this infiltration reaches a high degree in the pars papillaris, the epidermis is thinned, and the epidermodermal junctions flattened, and, at times, the epidermis is completely wanting. The section shows parakeratosis acanthosis.

The lesions varied in the amount of irritation. Six months ago a patch on the inner side of the left arm became bigger and ulcerated, and it now presents an everted edge, with a full pus-producing base. The patient had one hard gland in the axilla on the same side, and that was thought, clinically, to be epithelioma.

Treatment.—It is proposed to treat this case with radium.

Dr. MUENDE said he supposed this case fitted in with the diagnosis of mycosis fungoides, but it was, he thought, more like true lymphoblastoma, in that the papillary part of it was comparatively free of infiltration, and the deeper part of the dermis was composed of large endothelial cells and large cells of the lymphoblast type. Here the cell types were very uniform and resembled those in typical lymphoblastoma. It lacked the polymorphic infiltration so regularly found in mycosis fungoides.

Poikilodermia Atrophicans Vasculare.—G. B. DOWLING, M.D.

E. P., aged 24. The condition appeared first four years ago, across the nose and on the knuckles. Further areas which have by degrees become involved in the process are the scalp, neck, chest, and back, the outer aspects of the arms, in the form of bands, the forearms in patches, and the extensor aspects of the thighs in the form of broad bands. The condition is gradually enlarging its boundaries.

The spreading portion consists primarily of a network with white glistening atrophic strands. Later, the patches have changed, becoming either red and irritable, rough, dry, and in places covered with scales resembling those of ichthyosis, or in a few cases they have become at first dark blue like a bruise, and have then undergone a kind of central necrosis with subsequent ulceration. With the exception of one which is still open, the ulcerated lesions, which have only appeared in recent months,

have eventually healed, leaving a dense cicatrix surrounded by an irregular glistening white atrophic border with traces of the original reticular arrangement.

From time to time irritation is experienced in the older portions, with occasional slight swelling and redness; this is found particularly on the face in the early morning.

At present all stages can be seen; the oldest lesions consist of large rough dry areas, in which reticular atrophy can easily be seen, together with mottled pigmentation and many telangiectases. This type of lesion is best seen on the chest, back and neck, extensor aspects of the arms, and on the thighs. Reticular atrophy, diffuse redness and many telangiectases are present on the face, but here there is no obvious scaly roughness. Similar lesions are present on the hands, on the dorsal aspects of the metacarpo-phalangeal and inter-phalangeal joints as well as on the terminal phalanges. The lesions here bear some resemblance to those of lupus erythematosus. The initial stage is best seen on the thighs where the large bands are gradually extending downwards.

In addition to the poikiloderma, the patient suffers from perniosis of the legs.

Acne Scrofulosorum and Erythema Induratum associated with Arthritis (Poncet type).—H. W. BARBER, M.B.

Miss V. B., aged 18.

History.—Her father died from some disease of the kidneys, the nature of which I have not been able to ascertain. Her mother is alive and well. The patient herself is the middle child of three, the other two being reported healthy. She was in good health until, at the age of six, she contracted scarlet fever, which was followed by otitis media and cervical adenitis. Eight years ago she had diphtheria, complicated by some paralysis and myocarditis. Convalescence from this was protracted, and the pustular eruption, now present on the back, chest and face, began to appear while she was in hospital. During an attack of measles three-and-a-half years ago this completely cleared up, but reappeared in a few weeks. Tonsillectomy was performed four years ago, and both antra were irrigated a year later. The peri-articular swellings of the fingers developed after an attack of whooping-cough about eighteen months ago. The ulcerated lesions on the legs appeared at the beginning of last year; they healed during the summer, but relapsed in September. An interesting point is that the keratosis pilaris, which is present on the arms, thighs and legs, has been present for only two years.

Present condition.—The patient affords an interesting example of tuberculous allergy affecting the skin and peri-articular structures. On the face, neck, chest, and back is an extensive eruption of the acneiform tuberculide (acne scrofulosorum). The lesions vary in size, and consist essentially of inflammatory papules surmounted by pustules, which represent central areas of necrosis. Scarring naturally results, and, on the front of the chest particularly, small scars encircling the follicles are well seen. On the elbows are flat encrusted scars of considerable size, and some pustulo-necrotic lesions are present on the arms and hands. On the legs similar small lesions are seen, and on the lower parts—both front and back—are large encrusted ulcerated areas and numerous scars (erythema induratum of Bazin). There is well-marked keratosis pilaris of the arms, thighs, and legs, which appeared only two years ago.

Joints: Fusiform peri-articular swellings are present around the first inter-phalangeal joints of the hands, particularly of the middle fingers. The metacarpo-phalangeal joints are also involved. According to the radiologist's report, there are no bony changes. I am not in entire agreement with this, but at any rate they are not striking.

There are several palpable lymphatic glands in the posterior triangles of the neck, and one of considerable size in the left axilla.

Investigations.—Skiagram of chest: Median opacity normal; diaphragm moves evenly, not freely; costophrenic angles clear. Large fibrotic roots with several old foci at each, striation at right base. Positive Mantoux reactions were obtained to both tests with human and bovine tuberculin in dilutions of one in five thousand.

Discussion.—Dr. PARKES WEBER asked whether the "Poncet type" mentioned meant that the peri-arthritic swelling was due to the local presence of tubercle bacilli, or not.

Mr. H. CORSI said he did not feel satisfied about this case, as it made him think he had been diagnosing as acne vulgaris a number of cases with shoulder and face affected in much the same way. Was it essential that a person should have comedones for the diagnosis of acne vulgaris to be made? In cases of acne scrofulosorum he thought that the lesions were more inside the skin, and not so prominent as in this case.

Dr. BARBER (in reply) said he found it difficult, when searching the literature, to determine exactly what Poncet's conception really was; he thought he meant an arthritis or peri-arthritis occurring in tuberculous people, in which the condition in or around the joints was an allergic reaction to tuberculin. He (the speaker) regarded this case as of that nature. He thought the peri-articular changes were not due to the presence of bacilli, but were merely reactions to the tubercular toxin.

If Mr. Corsi would examine the lesions carefully, particularly those on the back, he would see that they differed from those of ordinary pustular acne. The lesions began as inflammatory papules, and a pustule formed in the centre, rather like the pustule of a papulo-necrotic tuberculide, though more superficial, and on removing the crust a sharply defined central area of necrosis was found lying beneath the pustule. Dr. Adamson agreed that in these cases the pustulation was different from that of pustular acne.

Urticaria Pigmentosa.—C. H. WHITTLE, M.D.

D. W., a man, aged 32, gives a history, of only six years' duration, of slightly itchy spots on the back and limbs.

The lesions, which are chiefly on the back and front of the chest, but are also present on the upper arms and thighs, are pigmented papules varying in size from that of a lentil to that of a split pea, around which the skin shows a tendency to flare and produce urticarial wheals on rubbing. The condition is not very itchy.

The irritability of the skin which gives rise to factitious urticaria appears to be limited to those parts on which the papules occur. No reaction is obtained on the forearms for instance.

The onset at the age of 26 seems unusually late, but there have been recorded other cases in which the condition appeared for the first time in adult life.

No biopsy has been obtained in this case.

Mycosis Fungoides.—H. C. SEMON, M.D.

Mrs. Florence R., aged 35.

History of present illness.—In 1926 patient first noticed a single red patch on one buttock. It was about 3 in. in diameter. Two months later a smaller patch appeared in the lower part of the back, and—while these did not disappear—two further small patches developed between the shoulder blades. There was no irritation at any time but as the patches did not clear up, she attended St. Bartholomew's hospital some time in 1929, and was under treatment there four and a half years for psoriasis. In June 1933 a course of 26 bi-weekly injections into the buttocks was begun, but neither this nor any of the other treatments given had any effect on the patches. Towards the end of the course of injections the whole skin began to peel, and when she appeared in the out-patient department at the Royal Northern Hospital, in November, the case was clearly one of acute generalized exfoliative dermatitis. The condition persisted with a swinging pyrexia up to 102° F. until the beginning of this year, when exfoliation diminished and infiltration, more or less pronounced over the whole body, took its place. On or about January 8 the

infiltrations gradually became more confluent, giving rise to the formation of definite raised tumefactions, soft in character and reddish in colour. Superficial ulceration has occurred in quite a number of them.

Patient has three daughters. All healthy. Nothing relative in family history; no psoriasis or other skin abnormality.

General health has always been good. No history of serious disease.

DIFFERENTIAL BLOOD-COUNTS.

	21.12.33		16.1.34	
P. ...	69%	2670	61%	648
L. ...	23%	690	27%	2160
L. mon.	3%	90	3%	240
Eos. ...	4%	120	9%	720
Mast cells	1%	30	—	

Histological report.—The section shows skin and subcutaneous tissue cut somewhat obliquely. There is a patchy, but massive infiltration of the subcutaneous tissues beginning immediately beneath the epidermis with cells of varying type. The chief cells are small and large round cells which resemble small and large lymphocytes. Polymophonuclears and eosinophils are sparsely scattered throughout. Plasma cells are present, and there are several cells showing mitotic figures. There is intense vascular congestion in places. Note the polymorphous structure of the infiltrate resembling a form of granulation tissue.

Discussion.—Mr. H. CORSI said he had seen this woman at St. Bartholomew's Hospital on and off for some years. She had, he believed, psoriasis, and in spite of the recent development of mycosis fungoides, he still thought she had psoriasis and not a premycotic eruption. She had received a number of injections of mercolloid.

The PRESIDENT said he had now under his observation a patient who when first seen, some three years ago, presented a generalized erythrodermia. After the exclusion of leukæmia, a tentative diagnosis of mycosis fungoides was made, and this was confirmed at a later stage when a number of flat tumours developed. These have cleared up under X-ray treatment, but the erythrodermia has recurred, and the condition is now one of general and severe exfoliative dermatitis without tumour formation.

ADDENDUM (27.3.34).—Systematic irradiation of the trunk and limbs (with X-rays) had a temporary effect in healing the ulceration of the tumours, but the patient became more and more feeble and emaciated, and died eventually in coma on March 2. Post-mortem examination revealed the effects of acute sepsis. There was a pyæmic abscess in the left kidney, fatty degeneration of the liver to some extent, and a large spleen. There was no evidence of metastatic deposit in any of the organs. A section of one of the cutaneous tumours was identical in all respects with that of the infiltration above described. [H. S.]

Ulcerating Keloid in an Infant.—H. MACCORMAC, C.B.E., M.D. (President).

The patient, a child, aged 1½ years, was first seen in December 1932: there was then present over the centre of the lower back an oval ulcerated surface 2½ in. across and 1½ in. vertically. The edges of the ulcer are raised, hard and of a brown colour, resembling keloid tissue. A small typical keloid is present at the side of the main lesion.

The parents state that they first noticed a raised patch at the age of six weeks; it remained unaltered until four months ago when the central portion became ulcerated, leaving a rim of hard tissue, and in this form it has persisted until the present time.

A microscopic section taken at the edge of the ulcer, shows an inflammatory cell reaction which is mainly subepidermal below which are dense bands of fibrous tissue, appearances consistent with a keloid, but inconsistent with a simple granuloma.

Ulcerating keloid.

This case presents unusual features. While keloids may develop at any age, they are rare in infancy and it is usually stated that ulceration never occurs. There are thus present, first, a keloid in an infant—it itself exceptional—and secondly, ulceration in a keloid which is among the rarest of dermatological phenomena.

Two Cases of Folliculitis Decalvans.—Sir ERNEST GRAHAM-LITTLE, M.D.

(I)—The patient, a woman, aged 42, has well-defined patches of psoriasis on the knees and three areas of cicatricial alopecia on the scalp. A curious feature of this case is the history of a free sudden loss of hair, the first indication of the trouble, dating from three months ago, being the finding of hairs upon her dressing gown.

Axillary and pubic hair normal. Some active follicular inflammation still present on the scalp.

(II)—The patient, a woman, aged 46, has cicatricial alopecia dating from two years ago, and now extensively involving the scalp. Axillary hair is normal; pubic hair is extremely scanty, but there is no cicatrical alopecia visible. There is also some inflammatory folliculitis still present.

Telangiectasia of the Face, Neck, and Arms, associated with Pregnancy.—LOUIS FORMAN, M.D.

Mrs. C. T., aged 32.

History.—She has been pregnant twelve times. The first child, a girl, is alive and well (now aged 10 years). The other pregnancies terminated about six weeks prematurely with a dead fœtus. The last child, however, lived five hours, and post-mortem examination showed fœtal ascites and jaundice.

During the last eleven pregnancies telangiectases have appeared on the face, the V-shaped exposed portion of the neck and the extensor parts of the forearms, at the end of the first month of pregnancy.

About five days after the delivery of the fœtus she says that the telangiectases disappear. During her last pregnancy she was in hospital under Mr. F. Cook. The Wassermann reaction was then found to be negative, but the lævulose tolerance test showed a definite liver deficiency. Such a finding is, however, not uncommon, I believe, with pregnancy.

She is now six months pregnant. There is a well-marked capillary telangiectasia affecting the whole of the face and the exposed part of the chest and, to a lesser degree, the backs of the forearms.

The possible causes of capillary dilatation during pregnancy would be (1) a functional disturbance of the liver (*cp.* capillary dilatation of the face with cirrhosis); (2) abnormality of function of the stomach (*cp.* rosacea); (3) ovarian dysfunction.

Discussion.—The PRESIDENT said that when he was a medical registrar, a young woman was twice admitted to hospital because of a gastric ulcer. On each occasion, while the symptoms of the ulcer were pronounced, numerous, stellate nævi appeared, mainly on the trunk, disappearing spontaneously as the gastric condition improved.

Dr. P. M. F. BISHOP said that possibly this might be a manifestation of the excessive secretion of œstrin which occurred during pregnancy. Throughout pregnancy this œstrin secretion was above that of the normal menstrual cycle, the maximum being reached at term. Within five days of the termination of labour the figure dropped to normal. The main functions of the œstrin were associated with the development of the extra-ovarian genital organs, i.e. the vagina, breasts, vulva, endometrium, etc., and in each of these cases that development was aided by a localized dilatation of the vessels supplying these organs. On seeing this woman he thought that the circulation in the capillaries was more sensitive than in normal women, and the reaction took the form of this vascular dilatation due to the excessive secretion of œstrin during pregnancy. There was probably a predominance of the œstrin over the progestin factor, which latter was supposed to be concerned with the maintenance of pregnancy to term.

Œstrin might be injected in this case to see whether it was possible to bring about this telangiectasia; also the dilatation of the skin capillaries could be tested by pressure applied round the arm during pregnancy, and again afterwards.

Dr. DOWLING said that stellate nævi were a common accompaniment of pregnancy.

Dr. PARKES WEBER thought such a condition of telangiectasia of the face and elsewhere with pregnancy must be a great rarity, and if it was due to œstrin, why should this woman be, perhaps, the only woman in the world to show such a telangiectasia, as all women had excretion of œstrin in pregnancy? Dr. Dowling's remark was much to the point, because many of the telangiectases were similar to stellate ones where several coalesced. He hoped that proof would be forthcoming that the lesions disappeared between pregnancies.

Dr. S. E. DORE said cases had been described—in America chiefly—of multiple telangiectasis in Graves' disease, though he did not know that this had any bearing on the present

case. He did not know of a case in which telangiectasia occurred in pregnancy and cleared up so quickly after it.

Dr. FORMAN (in reply) said that he had not verified the patient's statement that the condition completely cleared up between pregnancies.

The President's case of telangiectases of the face with gastric ulcer was of extreme interest. It might be that there was an inherited lability of the capillaries in these cases.

Section of Odontology

President—Sir NORMAN BENNETT, M.D., L.D.S.E.

[*January* 22, 1934]

A Case of Anidrotic Ectodermal Dysplasia showing Extensive Dental Defect

By MARTIN A. RUSHTON, M.B., B.CH., L.D.S.

THE type of dysplasia shown in the case which I am about to describe, and also known as major ectodermal defect, is a hereditary condition in which the affected persons are usually small and delicate, have no sweat glands and often no lachrymal glands, insufficient and conical teeth, fine fair hair, and chronic rhinitis leading to loss of the sense of smell. While the lack of teeth and hair does not greatly affect their activities, the absence of sweat prevents them doing any work in hot weather. The recorded cases of the condition, which is a rare one, have been summarized and analysed by Dr. E. A. Cockayne in his recent book on "Inherited abnormalities of the skin and its appendages." Two varieties of the defect have been distinguished according to the mode of inheritance. In one of these the abnormality is handed down as a sex-linked recessive character and in the other as an incomplete dominant.

John E., aged 4½ years.

Previous history.—His birth-weight was 6½ lb., but he did not put on weight for a long time. He suffered frequently from nose-bleeding between the ages of 11 months and 3½ years. At the age of 11 months his tooth erupted; he had whooping-cough at the age of 2 years, and he has always suffered from "catarrh of the nose and stomach." He never sweats at all and is apt to get exhausted when it is warm; if he gets hot, he just lies down wherever he may be and rubs his forehead as if he had a headache. He often asks for a bucket of water in summer and gets into it and dabbles about. He objects to sunlight and other bright lights, and always keeps in the shadow. He never had any tears until a few months ago, and still has extremely few.

Present condition.—He is 41 in. high, but weighs only 35 lb: is thin and of delicate appearance, active, cheerful, and intelligent. His hair is fine and fair, and there is quite a good covering of it, better in front; over the occiput it is fluffy; it is said to grow at the normal rate, being cut every three weeks. The eyebrows are very fair and downy; the upper eyelashes are normal. There are no lower eyelashes, and there is no hair on the limbs. The skin is dry and rather harsh, but not wrinkled; on the face it has a transparent look and there is no trace of sunbrown. There are dark purplish circles round the eyes, and the lips are very red. The nails are normal, and the eyes are pale blue. The cheeks are not sunken, but the mouth has a flabby look, no doubt due to the lack of teeth. There is only one tooth erupted; it is conical, resembling a deciduous canine tooth, and occupies the position of the right first upper incisor (fig. 1). Which tooth it represents it is difficult to say, since in other cases in which a number of incisors or canines have been present they have all had this same conical shape. Skiagrams show that the only other teeth are two half-formed conical unerupted ones in the right upper incisor region. There is an oval depressed area in the mid-line of the soft palate near its junction with the hard. The lower alveolar ridge is sharp and narrow. If the one erupted tooth is seized and waggled, considerable movement of the maxilla on the rest of the skull may be obtained.

Family history.—The mother is short and plump, with blue eyes, brown hair, freckles, and a rather saddle-shaped nose (she suffers from nasal catarrh, but has not lost the sense of smell). She thinks that she sweats less than other people and dislikes the heat. Her teeth are irregular, deformed, and insufficient. Of many only the roots persist; one has been extracted by a dentist and several she has

pulled out herself, but the exact number is unknown (fig. 2). The following remain: *Upper right.*—One molar, molar and premolar root fragments, a very small but normally shaped first premolar, canine and central incisor. *Upper left.*—A large conical tooth curved backwards (a type very characteristic of deformed permanent front teeth in this dysplasia), a broken-off tooth resembling a central incisor, and

FIG. 1

FIG. 2

two molars. *Lower right.*—Two molars, two premolars, canine and one conical tooth. *Lower Left.*—Canine, one premolar, and one molar. She thinks that she has never had any teeth in the upper and lower anterior gaps. Thus the mother shows a few of the characteristics of the dysplasia, the most definite being the

conical teeth. This is important when considering the mode of inheritance, since in the rest of the family tree the dysplasia seems to have behaved as a sex-linked character, and no other female relatives are known to have been affected (fig. 3).

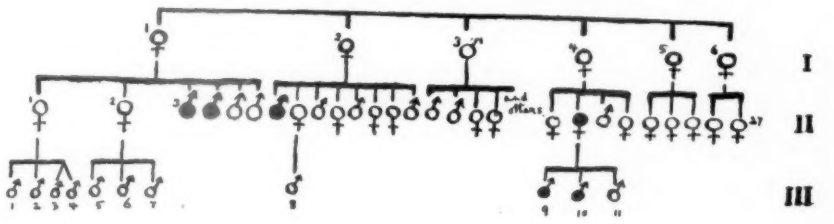

FIG. 3.

There are no consanguineous marriages.

I. 3. Condition unknown. Position among sibs not quite certain.

II. 3 & 4. Very fair, hair scanty, good height; one is thin. Do not sweat, and cannot work in hot weather. Like John but not in such good condition. Only had a few teeth; "one now and again" (aged 22 and 21).

II. 7. Just the same as above except that he had "plenty of teeth."

II. 15 to 18, etc. A large family; black hair and good teeth.

II. 20. John's mother, has a few missing and conical teeth.

III. 9. John's brother, died of bronchopneumonia at five weeks. Was like John, very fair and "no proper gums."

III. 10. John, born two years after above.

III. 11. Another brother, died of bronchopneumonia at 3 weeks. Was dark and had normal gums. Was born two years after John. (Pedigree constructed on evidence of II. 20. Only II. 20 and III. 10 examined.)

It is possible that some of the members marked as normal possessed minor dental abnormalities, but as the family is scattered this cannot be determined.

From the pedigree it appears that the only members severely affected are males descended from three sisters, and that the defect was transmitted to the third generation through the female. The fact that the mother of my patient showed some of the signs of the condition, however, makes it clear that the inheritance was not of strictly sex-linked recessive type.

Treatment.—As regards treatment, the only part which concerns us is the making of an attempt to avoid the development of the unsightly facies which accompanies this dysplasia in adult life. Dr. Cockayne writes:—

"The expression is peculiar, owing to the sunken cheeks, short upper lip, pointed chin, thick lips, and saddle-shaped nose. The depressed bridge of the nose is due to the destruction of bone by the chronic rhinitis, but the other facial characters are secondary to the absence of teeth, which prevents the proper development of the maxillæ and alveolar margins of the jaws. The lips are thick from compensatory hypertrophy. If some front teeth are present the alterations of contour are much less pronounced."

This facies could, perhaps, be partly prevented, especially as regards the hypertrophy of the lips, by the early provision of dentures; and I should like to have the opinion of members as to how early a child can be induced to wear a full lower denture. I saw in the report of the school medical officer of Carlisle that school children there under the age of 13 years were wearing complete dentures, but no doubt it is possible to begin even earlier than this.

The Reaction and Regeneration of Cementum in Various Pathological Conditions[1]

By H. H. Stones, M.D., M.D.S., L.D.S.E.

Abstract.—(1) The reaction of cementum and its adjoining tissues to induced pathological conditions associated with the gingival sulcus is described.

(2) After subjecting the sulcus to interference, its histological appearance is compared with that of definite parodontal disease.

(3) Various methods were adopted for these experiments, which were performed on monkeys.

(4) Artificial pockets were produced by detaching the subgingival epithelium and underlying connective tissue from the cementum. Results: (*a*) Cementum is easily removed accidentally, when scraping monkeys' teeth. (*b*) Reattachment of connective tissues to cementum is effected, but is usually incomplete. (*c*) Epithelium always firmly reunites with cementum. (*d*) The artificial sulcus which is usually deeper than normal does not show, microscopically, the same pathological changes as in parodontal disease.

(5) In other experiments, in addition to deepening the sulcus, the cementum lining the pockets was also removed, leaving denuded dentine in contact with the connective tissue. A similar condition was achieved by another method in which a dental bur was inserted between two teeth below the gum margin.

Results: (*a*) The gingival epithelium is capable of forming a weak attachment to the dentine, though this does not usually occur. It always proliferates down and unites with the nearest layer of cementum. It seems to have a peculiar affinity for this tissue. (*b*) Underlying connective tissue does not usually unite with the dentine. When this happens it is effected by the regeneration of cementum, this new tissue being lined by new cementoblasts. (*c*) The width of the periodontal membrane, which was increased by the experiment, is reduced to a more normal level by deposition of new alveolar bone, and to a lesser extent by regeneration of cementum. (*d*) In this series of experiments the artificial pocket is permanent and somewhat resembles that of parodontal disease. This is probably due, not so much to the injury, but to its effects creating a space which forms an area of chronic stagnation.

Résumé.—(1) Description de la réaction du cément et des tissus adjacents aux conditions pathologiques expérimentales du sulcus sous-gingival.

(2) L'histologie du sulcus après certaines interventions est comparée à celle dans les affections parodontales.

(3) De différentes méthodes ont été employées pour ces expériences chez le singe.

(4) Des poches artificielles furent formées par le détachement de l'épithèle et du tissu conjonctif sous-jacent du cément. Résultats: (*a*) Le cément se détache facilement accidentellement quand on gratte les dents chez les singes. (*b*) Le tissu conjonctif se rattache au cément, mais d'habitude incomplètement. (*c*) L'épithèle se rattache toujours solidement au cément. (*d*) Le sulcus artificiel, généralement plus profond que sous les conditions normales, ne présente pas les mêmes altérations pathologiques que dans les maladies parodontales.

(5) Dans d'autres expériences, en plus de l'approfondissement du sulcus, le cément revêtissant les poches fut enlevé, et la dentine exposée au tissu conjonctif. Des conditions semblables furent obtenues par une autre méthode, une fraise étant introduite entre deux dents, sous le bord de la gencive. Résultats: (*a*) L'épithèle des gencives peut s'attacher faiblement à la dentine, mais ceci n'arrive pas d'habitude. Il se prolifère toujours et s'attache

1 The writer wishes to express his gratitude to the Medical Research Council and the Dental Advisory Committee, who have generously assisted this investigation by means of a grant.

à la couche la plus rapprochée du cément. L'épithèle paraît avoir une affinité spéciale pour le cément. (*b*) Le tissu conjonctival sous-jacent ne s'unit pas d'habitude à la dentine. Si l'union se fait elle est produite par la régénération du cément, et le tissu neuf est revêti par de nouveaux cémentoblastes. (*c*) La largeur de la membrane périodontale, augmentée par l'intervention, rentre dans des limites plus normales par la formation d'os alvéolaire, et à un moindre degré par la régénération du cément. (*d*) Dans ces expériences la poche artificielle reste permanente, et ressemble un peu à celle des affections parodontales. Ceci est probablement dû à la production d'un espace formant une région de stagnation chronique, plutôt qu'au traumatisme.

ZUSAMMENFASSUNG: (1) Die Reaktion des Cementum und der benachbarten Geweben auf experimentell erzeugten pathologischen Zuständen des Zahnfleisch Sulcus wird beschrieben.

(2) Das histologische Bild nach den Eingriffen wird mit dem Bild der deutlichen Paradentiumerkrankungen vergleicht.

(3) Es wurden verschiedene Methoden für diese Versuche mit Affen angewandt.

(4) Künstliche Taschen wurden durch Abtrennung des subgingivalen Epithels und des darunter liegenden Bindegewebes von dem Cementum erzeugt. Ergebnisse: (*a*) Das Cementum kann leicht unerwünscht entfernt werden wenn man die Zähne von Affen kratzt. (*b*) Das Bindegewebe wächst wieder an das Cementum, aber gewöhnlich nur unvollkommen. (*c*) Das Epithel wächst immer wieder fest an das Cementum. (*d*) Der artefizielle Sulcus, der etwas tiefer ist als normal zeigt nicht dasselbe mikroskopische Bild wie bei Paradentiumerkrankungen.

(5) In weiteren Versuchen wurde der Cementum Besatz der Taschen entfernt, sowohl als der Sulcus vertieft, und die entblösste Dentin in Berührung mit dem Bindegewebe gelassen. Ein ähnlicher Zustand wurde durch eine andere Methode erzeugt, indem ein Bohrer zwischen swei Sähne unter dem Zahnfleischrand eingeführt wurde. Ergebnisse: (*a*) Das Zahnfleischepithel kann schwach mit der Dentin zusammenwachsen; dies geschieht jedoch gewöhnlich nicht. Das Epithel wuchert immer nach unten und wächst mit der nächsten Cementumschicht zusammen. Das Epithel scheint eine besondere Affinität für dieses Gewebe zu besitzen. (*b*) Das darunter liegende Bindegewebe scheint mit der Dentin gewöhnlich nicht zusammen zu wachsen. Wenn dies geschieht kommt es durch Regeneration des Cementums zustande, wobei das neue Gewebe von neuen Cementoblasten besetzt ist. (*c*) Die paradentale Membran, die durch den Versuch erweitert ist, wird durch Ablagerung von neugebildetem Alveolarknochen, und in geringerem Grade auch durch Regeneration von Cementum, wieder zu einer mehr normalen Breite gebracht. (*d*) In dieser Versuchsreihe ist die Paradentiumtasche bleibend, und ist der Tasche in Paradentiumerkrankungen etwas ähnlich. Dieser Zustand hängt wahrscheinlich mehr von der Bildung eines Hohlraums welches eine Stelle von chronischer Stauung darstellt, als von der Schädigung selbst.

IT has already been shown that in the adult dog primary cementum which surrounds the upper part of the root is completely impermeable to dyes. By similar methods to those used by Fish [1] in his investigations into the permeability of dentine, this conclusion has been reached by Ross [2] who immersed freshly extracted teeth in methyl blue, and by the writer, working with various dyes *in vivo*. In regard to mature secondary cementum containing cells, it was found that from the dentine this variety was only penetrated at the apex. These cells, however, particularly in the outer layers, are permeable from the periodontal membrane. Thus the tissue that is being considered is such that the primary variety is even more impermeable than enamel, and has no lymph communication with the adjoining structures, while the newest or outer layers of the secondary type maintain vital communication with the periodontal membrane. The importance of cementum can be realized when it is seen that it is intimately associated with the following two types of dental disease, either of which in turn may cause various pathological systemic conditions:—

(1) Infection from within the tooth. Here any such infection is completely cut off from the surrounding tissues by the impenetrable cementum, except at the lower

end of the root, where it may pass not only through the blood-vessels but also through the cementum which is permeable in this region, resulting in apical sepsis.

(2) Infection of the tissues surrounding the tooth, or paradontal disease. In this condition the epithelium and underlying connective tissue gradually recedes or is slowly detached from the cementum, and at the same time there is a concomitant destruction of the crests of the alveolar bone. The changes in the surrounding tissues have been already described [3]. It should, however, be noted that the only part of the tooth associated with this disease is the cementum.

The object of the present investigation has been to determine the rôle of this tissue in various pathological conditions, particularly those associated with the gingival sulcus. This has necessarily involved a consideration of some reactions of its adjoining tissues, both the dentine and the soft tissues attached to its outer surface. Pockets have been experimentally produced in some cases, a few months afterwards the jaws and teeth being examined to compare their histological condition with that of a definite parodontal infection. Such a comparison is of value when considering the ætiology of the latter disease, and whether it is due to local conditions in the mouth or to some general systemic disturbance: for here not only has the initial lesion of this disease—detachment of the epithelium from the cementum—been produced, but the underlying connective tissue has also been severed from the tooth to insure the artificial pockets being of sufficient depth. In other cases the possibility of re-attachment of the surrounding tissues to cementum and denuded dentine, and the regeneration of cementum on the latter have also been investigated. These questions are clinically of importance when considering the merits of certain methods of treating gingival infections such as that advocated by Box [4], and the surgical elimination of pockets.

Method.

Experiments, which were carried out on monkeys, will be considered under two headings.

(1) Detachment of the subgingival epithelium and underlying connective tissue from the cementum: The technique adopted consisted in detaching these structures from the tooth on either the labial or lingual surface for about 2 mm. or 3 mm. and thus creating an artificial pocket by increasing the depth of the gingival sulcus to this extent. Experiments were carried out under a mixture of ether and chloroform, using a junker apparatus, and were terminated at varying periods of time from eleven to forty weeks. Serial sections were prepared by the butyl-alcohol method and were examined: (*a*) to see if reattachment were effected or not; (*b*) to compare the histological condition of the tissues with that of definite parodontal disease.

(2) Removal of cementum from the underlying dentine: In this series of experiments not only were the epithelium and underlying connective tissues detached from the tooth as above described, but the cementum lining the artificial pocket was also scraped away with a small dental fissure bur.

Another method was also adopted in which Dr. Wilfred Fish collaborated with the writer. Here a fissure bur was inserted through the gum between two teeth about 2 or 3 mm. below the papilla. By this means a groove was cut in both teeth under the gum, removing the cementum and part of the dentine. Sections were again prepared to examine the tissues and in particular to determine whether: (*a*) The subgingival epithelium was capable of reattachment to the denuded dentine; (*b*) underlying connective tissue effected union with the dentine; (*c*) new cementum were regenerated on the dentine; (*d*) any effects were produced on the adjacent alveolus.

Results.

(1) In the first series of experiments in which the gingival sulcus was merely deepened by detaching the soft tissues from the tooth, it was observed that the cementum also was frequently accidentally removed (figs. 1 and 7). This was unexpected, as it had not been realized that the cementum could be so easily detached, and this would seem to be an important practical observation in connexion with scaling the teeth of man. In this operation, as is known, not only should the superficial salivary tartar that coats the enamel be scraped away, but also the hard subgingival

× 19

FIG. 1.—Experimental deepening of labial gingival sulcus (S) by detachment of the subgingival epithelium and underlying connective tissue from the tooth. Monkey. Condition after twenty-eight weeks. Cementum (C) which is easily damaged has been accidentally removed. The underlying connective tissue (C.T) has not united with the denuded dentine (D), but is separated from it by a downgrowth of epithelium (E). The latter has proliferated towards and united with undisturbed cementum.

calculus which collects between the teeth and at the bottom of the gingival sulcus. In this position it is often firmly attached to the cementum. It is very important that these deposits should be carefully and thoroughly removed for both the prevention and the treatment of parodontal disease. A detailed technique for scaling is taught by some schools abroad, including the use of abrasive carborundum strips to remove any remaining débris between the teeth—the gum having been previously anæsthetized. The ease with which the cementum can be removed in

the monkey indicates that greater care should be used when scaling the teeth in man and that hard abrasives that may come in contact with the cementum are contra-indicated.

Histological examination showed that, occasionally, complete reattachment of the epithelium and underlying connective tissue to the cementum was effected. Often but little difference from normal could be seen on comparison with untreated control teeth (fig. 2). This re-attachment was found to be weak, even after thirty

× 112

FIG. 2.—Experimental deepening of lingual gingival sulcus (S). Monkey. Condition after twenty-one weeks. The epithelium (E) and underlying connective tissue (C.T) have effected complete re-attachment to the cementum (C). The latter has been accidentally damaged at "X" and is being regenerated. Signs of inflammatory reaction have disappeared.

weeks, as it was very much more frequently torn on cutting sections than the control side. The epithelial attachment in these specimens was fairly normal and signs of inflammatory reaction had disappeared (fig. 3). In the majority of cases, however, it was found that the connective tissues obtained only partial reattachment to the cementum. Here the epithelium proliferated down over the detached connective tissue until the region was reached where the latter firmly united with

the cementum (fig. 4). Osteoclasts are occasionally found embedded in the cementum at the zone of operation. It is rather difficult to explain these variable results, as they do not seem to be determined by the age of the animal. The only explanations that can be offered are: Firstly, that it seemed to depend upon whether the cementum was damaged or not; reattachment was more easily effected if it

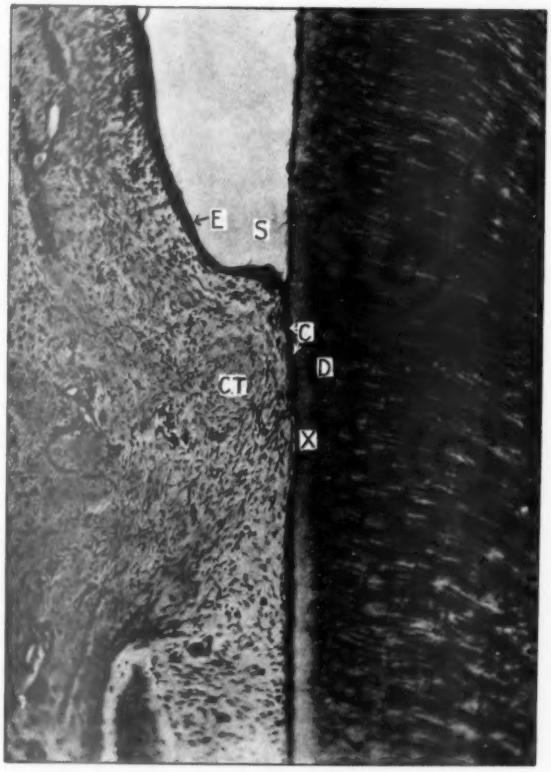

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FIG. 3.—Experimental deepening of labial gingival sulcus (S). Monkey. Condition after nineteen weeks. The epithelium (E) has united normally with the cementum (C). The latter has been accidentally damaged at "X." The underlying connective tissue (C.T) has united with both cementum and abraded dentine (D) Signs of inflammatory reaction have disappeared.

were uninjured. Secondly, consideration must be given to the factor of individual resistance to infection, as no aseptic precautions were taken when detaching the tissues.

Comparing the zone of operation with the pocket in parodontal disease, it is seen that none of the typical pathological changes associated with the latter are usually observed in the experiment. This is a factor of ætiological significance in

regard to this infection, for here not only has its initial lesion—detachment of the subgingival epithelium from the cementum—been experimentally produced, but the condition has been carried further by also detaching the underlying connective tissue. The result has been either complete or partial reattachment, otherwise the tissues appear fairly normal. The epithelial proliferation and typical round-celled

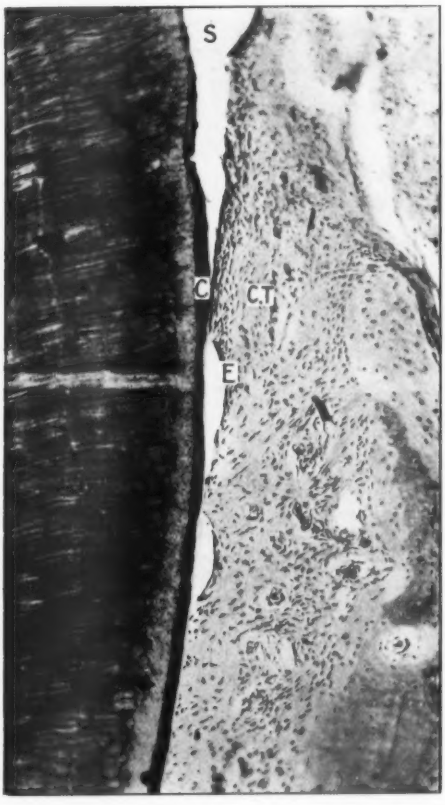

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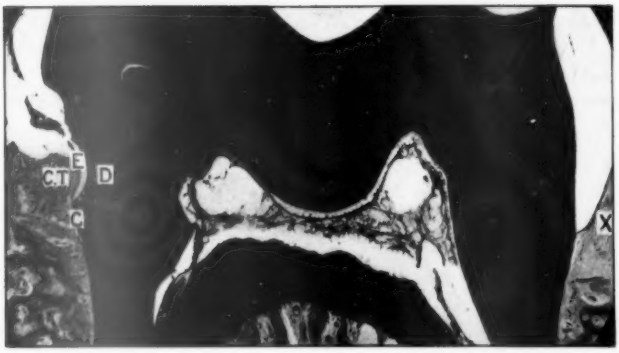
FIG. 4.—Experimental deepening of labial gingival sulcus (S). Monkey. Condition after twenty-one weeks. The underlying connective tissue (C.T) has obtained only partial re-attachment to the cementum (C). Epithelium (E) is growing down over the connective tissue that is detached from the cementum.

infiltration significant of chronic infection and associated with parodontal disease is practically absent. If such a potent local agent as the one associated with this experiment has not caused the latter infection, it offers evidence that there is some unknown factor, absent in the monkeys that were used, the presence of which, in conjunction with the local experiment, would have caused the disease. While it



× 11

FIG. 5.—Experimental removal of cementum and part of dentine by inserting a bur between the teeth, below the gingival sulcus. Monkey. Condition after thirty-eight weeks. The subgingival epithelium (E) has proliferated down over the underlying connective tissue (C.T), usually not uniting with the denuded dentine (D), until it reaches and firmly unites with the cementum (C). The control side is seen at X.

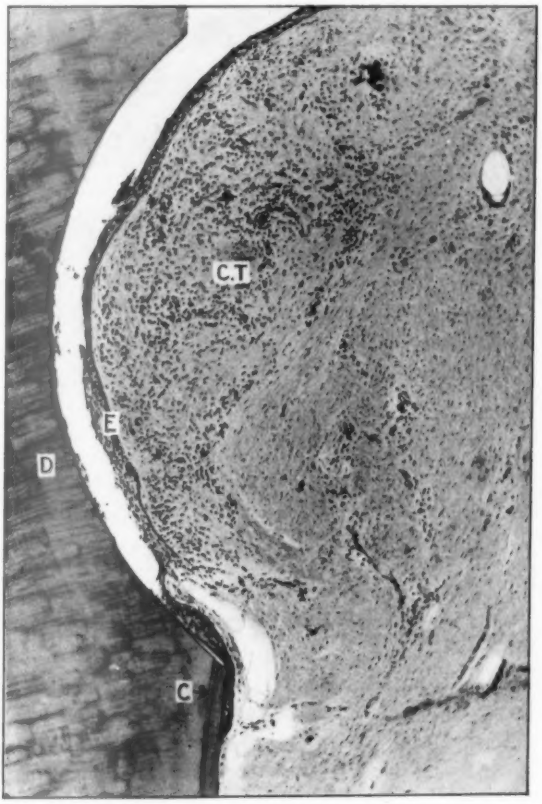


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FIG. 6.—Experimental removal of cementum as in fig. 5. Monkey. Condition after twenty-one weeks. The epithelial band (E) has formed a weak union to the dentine (D) which has torn, and a firm attachment to the cementum (C). The underlying connective tissue (C.T) is infiltrated with lymphocytes and plasma cells.

is not justifiable to deduce immediately that this missing factor is systemic in origin—for many cases of parodontal disease in man can be definitely explained by local conditions—it is possible and the result is interesting.

(2) In the series of experiments in which the cementum was burred away from

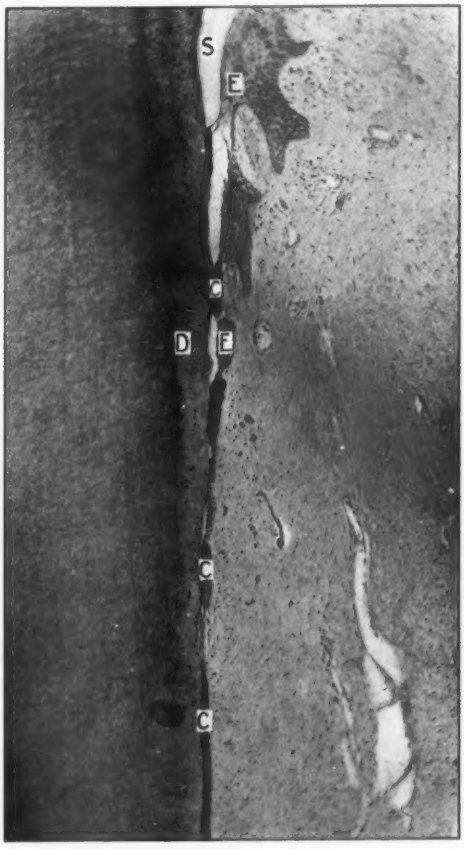

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FIG. 7.—Experimental deepening of labial gingival sulcus (S) by detaching the subgingival epithelium and underlying connective tissue from the tooth. Monkey. Condition after twenty-eight weeks. In this experiment pieces of cementum were accidentally removed. The subgingival epithelium (E) has proliferated down over the denuded dentine (D) and the remaining fragments of cementum (C), until the main undisturbed layer of the latter has been reached. Cementum is being regenerated over these fragments.

the dentine, either at the gingival sulcus or below the gum margin between the teeth, it will be necessary to consider the reaction of the various tissues separately.

(*a*) The subgingival epithelium. This invariably creeps down over the connective tissue until either undisturbed or regenerated cementum is reached, thus

separating the underlying tissues from the denuded dentine. Usually it does not unite with the latter (figs. 5 and 6). In certain cases odd fragments of cementum were left intact on the dentine, and the epithelium always became attached to these pieces, but continued proliferating down until the main vital layer was reached (fig. 7). Less frequently the epithelium definitely unites with the dentine on its downward course, but even then it continues and seeks the cementum. This was most usually observed in the cases in which a bur was inserted between the teeth (figs. 8 and 9). The union is

× 13

FIG. 8.—EXPERIMENTAL removal of cementum as in fig. 5. Monkey. Condition after nineteen weeks. The subgingival epithelium (E) has proliferated down over the underlying connective tissue (C.T) until it reaches and firmly unites with the cementum (C). In this section it has united with the denuded dentine (D). There is much infiltration with lymphocytes and plasma cells at the zone of operation when compared with the control tooth (X).

however weak and, from the examination of serial sections, easily torn (fig. 10). Thus epithelium seems to be attracted to cementum with which it is capable of firmly uniting. A further example of the attraction of epithelium to cementum is shown when a piece of the latter which has been detached is embedded in the gum and when the epithelium proliferates towards it (fig. 11). Sometimes these odd fragments of cementum remain in the gum near the denuded dentine. In this case they become surrounded by and embedded in the epithelium that is proliferating to the main

undisturbed cemental layer (fig. 12). Another interesting occurrence on this point is that in certain cases cells resembling cementoblasts have been seen lining the outer side of the new subgingival epithelium, these cells being thus interposed between the latter and the connective tissue (fig. 13). This affinity of epithelium

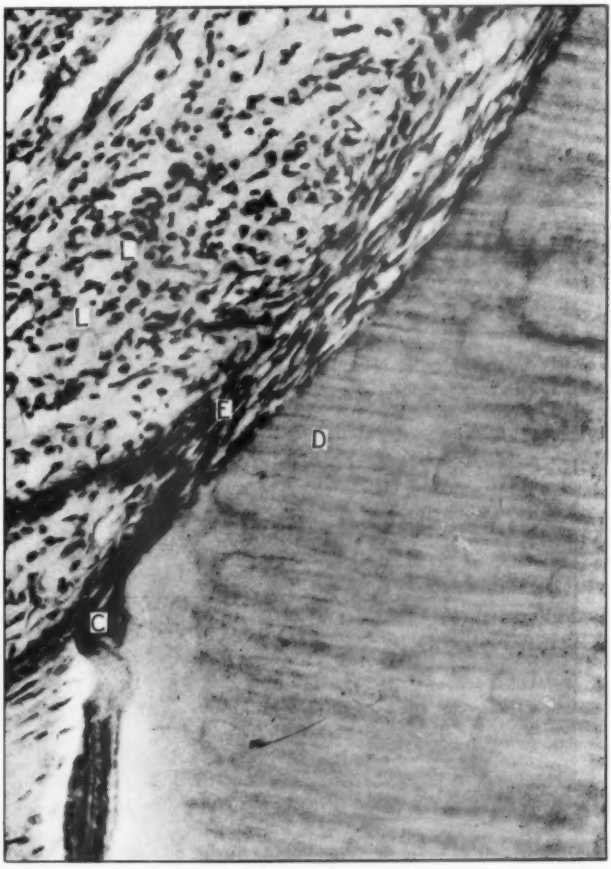

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FIG. 9.—Higher magnification of fig. 8. The subgingival epithelium (E) proliferating over and effecting attachment to the denuded dentine (D), has united with the cementum (C). Lymphocytes and plasma cells (L).

to cementum would explain Kronfeld's observation that the development of cementicles occurs close to epithelial rests [5].

These results substantiate the writer's experiments on gingivectomy in dogs, in which it was found that the epithelium covered the exposed connective tissue and united with the cementum one month after operation [6].

× 23

FIG. 10.—Experimental removal of cementum as in fig. 5. Monkey. Condition after thirty-eight weeks. The subgingival epithelium (E) has proliferated down over the underlying connective tissue (C.T) until it has reached the cementum (C). It has formed a weak and easily torn union with the dentine (D).

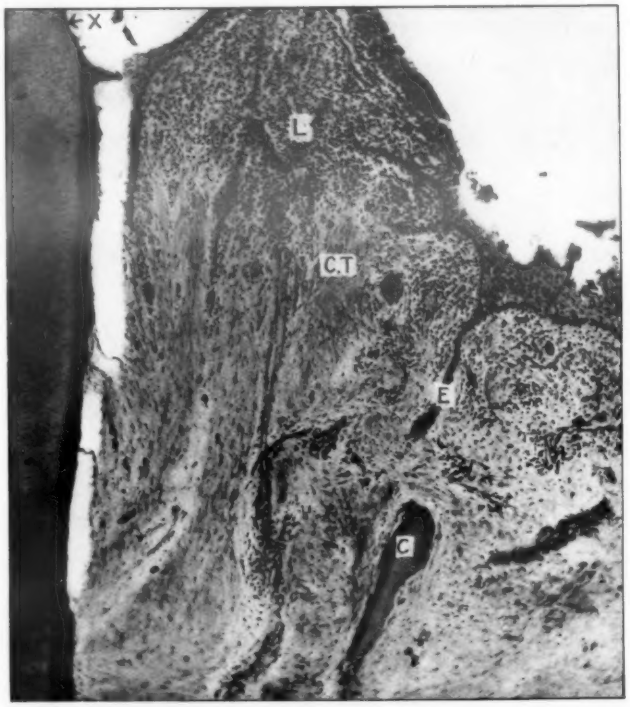

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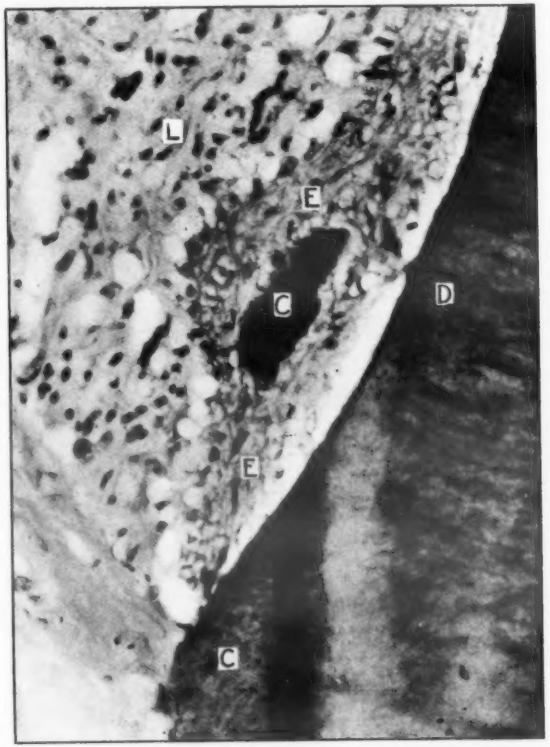
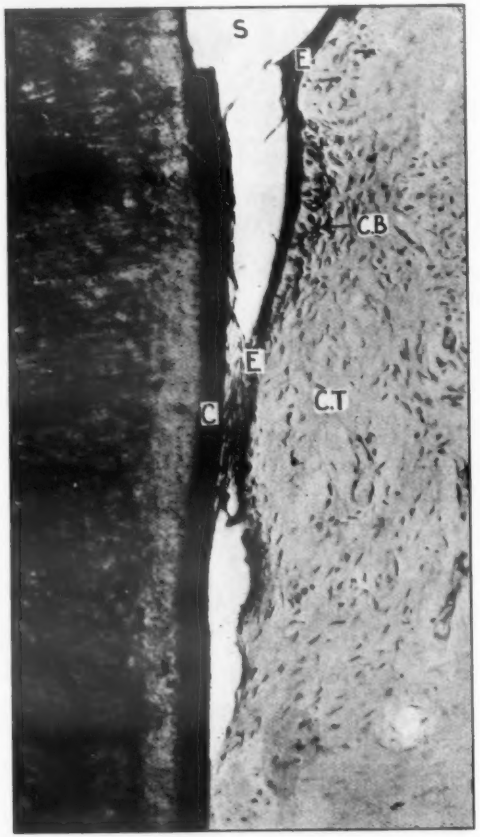
FIG. 11.—Experimental removal of cementum as in fig. 5. Monkey. Condition after twenty-three weeks. The tissues were removed at (X). A piece of detached cementum (C) has become embedded in the gum and a band of epithelium (E) is seen proliferating towards it. The underlying connective tissue (C.T) is infiltrated with lymphocytes and plasma cells (L).



× 360

FIG. 12.—Experimental removal of cementum as in fig. 5. Monkey. Condition after thirty-eight weeks. The subgingival epithelium (E) has proliferated over and weakly united with the denuded dentine (D) and joined the cementum (C). It has completely surrounded a detached piece of cementum. Lymphocytes and plasma cells (L).



× 180

FIG. 13.—Experimental deepening of labial gingival sulcus (S), the cementum lining the artificial pocket being scraped. Monkey. Condition after twenty-one weeks. The subgingival epithelium (E) has proliferated along and obtained attachment to the cementum (C). The underlying connective tissue (C.T) has not united with the latter in the upper part of the pocket. Peculiar cells resembling cementoblasts (C.B) are seen lining the outer side of the epithelial proliferation.

(*b and c*) The question whether the detached underlying connective tissue can effect union with the denuded dentine and the subject of regeneration of cementum will be dealt with together. This is a point of crucial importance when considering what success may be achieved from the ingenious re-attachment operation for parodontal disease practised abroad [4]. In this treatment the lining of the pockets, the cementum on the tooth and the subgingival epithelium, are scraped away leaving the exposed connective tissue in contact with the dentine, so that a case is presented which is very similar to these experiments except that the latter have the advantage of being

× 15

FIG. 14.—Experimental deepening of labial gingival sulcus (S), the cementum lining the artificial pocket together with part of the dentine being also removed. Monkey. Condition after twenty-one weeks. New cementum (C) has been regenerated on the dentine (D) only at the base of the injury, the connective tissue (C.T) being by this means re-attached to the denuded dentine. The subgingival epithelium (E) is proliferating as a smooth band to the new cementum. New alveolar bone (A) has been deposited to reduce the widened periodontal membrane (P.M) to its original dimension.

formed on young and previously healthy tissues. The results obtained do not support the efficacy of this operation, for when the cementum was removed over a large area in no case was there complete re-attachment of the connective tissue to the dentine, the artificial pocket being permanently deeper than the sulcus on the control cases. Partial re-attachment is frequently observed and the usual site is at the base of the pocket or injury (fig. 14). In all cases any successful re-attachment is accompanied by the regeneration of cementum on the dentine (figs. 15 and 16). If any

fragments of cementum have been left in situ formation of fresh layers of this tissue is encouraged. The new tissue, which is of the primary variety, such as had been removed, is lined by a regular row of cementoblasts (fig. 17). Speculation in regard to the origin of the latter is interesting, as the usual cementoblasts that line undamaged cementum have been completely destroyed in the experiment. The only conclusion that can be reached is that the contact of dentine or damaged cementum against the connective tissue of the periodontal membrane activates the adjoining cells of the latter and converts them into cement-forming cells.

(*d*) Effects on the adjoining alveolus. When the cementum is burred from the dentine below the gingival sulcus, the space between the tooth and the alveolus is much increased. At first the latter undergoes a sympathetic reaction and is absorbed by

× 14

FIG. 15.—Experimental deepening of labial gingival sulcus (S), the cementum lining the artificial pocket being scraped. Monkey. Condition after twenty-one weeks. The subgingival epithelium (E) and underlying connective tissue (C.T) have effected re-attachment to the abraded cementum (C) in the upper part of the injury. The cementum and part of the dentine (D) were removed at (X). Here there is only partial re-attachment

osteoclasts. Following this there is regeneration by osteoblasts, and new bone is formed to reduce the excessive gap between the tooth and alveolus. In fact it would seem that there is always an endeavour to maintain the periodontal membrane at its normal width, and should an acute condition supervene that threatens to destroy this equilibrium, the latter is maintained by the absorption or deposition of new alveolar bone. This achievement is sometimes further aided by the regeneration of cementum on the tooth surface.

Comparing the histological condition found in this group of experiments with that in parodontal disease, it is seen that the pathological changes

in the epithelium and underlying connective tissue are varied, for a distinct difference is noted between those cases in which the gingival sulcus was deepened with removal of the cementum and those in which a bur was inserted between the teeth. In the former it has been recorded that the new gingival sulcus is permanently much deeper than the control cases. As a result it might have been expected that the soft tissues would show the usual changes seen in chronic infection of the gum margin, but this is not so. Usually there is no marked epithelial proliferation either into the underlying connective tissue or along the cementum. There may be a certain infiltration of the tissues with lymphocytes and plasma-cells, but not to the extent seen in the usual case of parodontal disease. In the

× 315

FIG. 16.—Higher magnification of fig. 15. Intact original cementum (C) is standing in one part. New cementum (C.2) has been regenerated on the denuded dentine (D) and is lined by a regular row of cementoblasts (C.B).

bur-between cases a picture is presented that seems more to resemble the appearance of typical chronic infection at the gum margin. There is proliferation of the epithelium into the underlying connective tissue. A certain prolongation of this tissue is also seen along the cementum, though it is not nearly so marked as in the above disease. A comparable condition is observed in the round-celled infiltration of the tissues which is situated well above the epithelial attachment to the cementum. The explanation of these variable results is that in the latter experiments, which were carried out on posterior teeth, the injury itself leaves a marked interdental

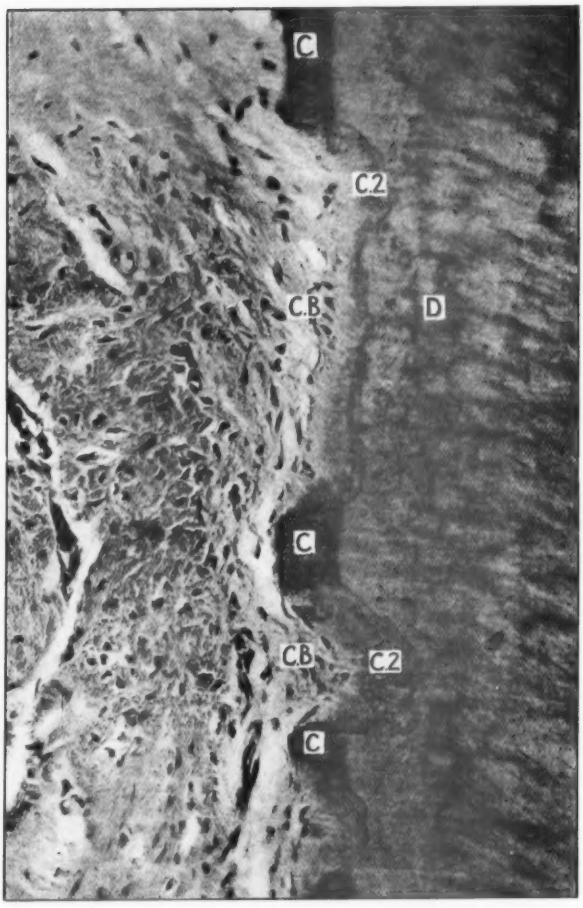


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FIG. 17.—Higher magnification similar to fig. 15. Condition after twenty-eight weeks. Original cementum (C) is standing in certain parts. New cementum (C.2) has been regenerated on the denuded dentine (D) and is lined by a regular row of cementoblasts (C.B).

space, thus forming an area of chronic stagnation in which food débris and bacteria become more or less permanently lodged.

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Section of Laryngology

President—MUSGRAVE WOODMAN, M.S.

[*February* 2, 1934]

The Innervation and Vascular Supply of the Antrum.

By CECIL STRONG.

ABSTRACT.—An attempt has been made to obtain information about the condition of the pulp of teeth, immediately below the bony incision, made in the lateral antral wall in radical antrotomy, and to investigate the conditions obtaining in the vascular supply of that neighbourhood.

The investigation has two parts: (1) Experimental; (2) Clinical.

Experimental.—(*a*) Injections of specimens of the superior maxillæ were made with lipiodol, then X-rayed. These showed vascular anastomoses along the antral floor.

(*b*) Sections of the lateral antral wall and floor were cut and stained to show nerves and blood spaces.

(*c*) The external carotid artery was injected with Prussian Blue and the maxilla then removed.

(*d*) Transverse sections of the teeth denervated were cut and their pulps examined.

Clinical.—The patients who had been submitted to operation were taken, and their teeth examined by:—

(*a*) Transillumination. (*b*) Percussion. (*c*) Thermal tests. (*d*) Faradic currents. (*e*) Radiography. From these investigations it appears that the teeth are denervated but not devitalized by the trauma to the lateral antral wall above their apices. Their blood-supply is still present, and probably comes through a collateral anastomosis, along the antral floor and partly through the antral mucosa.

THIS short paper represents a research into the condition of the teeth after the operation of radical antrotomy, as some uncertainty has existed as to whether the teeth:—

(1) Recover their sensation: (2) remain insensitive, or (3) are dead, and therefore subject to increased risk of caries, periodontal disease and apical abscess.

The upper teeth are supplied by the maxillary division of the fifth nerve, and the channels in the antral wall which accommodate such nerves are said to be injured by the operation of radical antrotomy. The teeth below the bony incision are said to be devitalized by this procedure, and it is in order to test the accuracy of this statement that this investigation has been undertaken, because if this is not so a grave objection to this operation disappears.

The investigation is divided into two parts:—

(1) A clinical examination of the patients' teeth in thirty-three cases after this operation.

(2) Determining where the nerve canals run to individual teeth, and the vascular supply to these teeth.

Clinical.—When the upper teeth of these patients are examined at periods varying from four days to three years after operation, certain members of the series are found to be anæsthetic. Usually these teeth are the first and second premolars and the first molar.

The methods of testing used were: (1) Application of cold by means of ice; (2) application of heat by a hot instrument; (3) stimulation with a weak Faradic current; (4) percussion.

The first of these methods was found to be the most reliable. The patient failed to appreciate the cold even after some thirty seconds' exposure. In all cases examined, there was this anæsthesia in at least one tooth, and sometimes in three teeth. The striking fact about these teeth is that, were it not for this test they would have been passed as normal. Their enamel was not discoloured, the gum was not retracted, and they showed no sign that there was anything wrong with them. It was this fact which caused the doubt as to whether they were really dead teeth, as certain colleagues would have us believe.

The number of teeth which suffer depends upon the size and position of the antral opening, and it will be seen from the skiagram that quite a small opening will cause the loss of sensation in one tooth only. In a case of bilateral antral polypi, different sized openings were made on the two sides, and the affected teeth ascertained. The small opening affected one tooth, and the large three teeth. This lack of sensibility in the teeth appears to be permanent. They remain anæsthetic.

Two facts also should be noted :—

(1) They show no X-ray change. (2) On transillumination they do not show that opacity which characterizes dead teeth and signifies a change in the enamel.

In view of the small changes noticeable in these teeth, is it not possible that they have been denervated by the operation but not necessarily devitalized? If their blood-supply has been impaired by the operation, has there not been a collateral circulation established, and are they not in fact still living?

It is with these questions in view that the second part of the investigation was carried out, an attempt to determine the vascular channels subservient to these teeth.

Technique.—A series of superior maxillary bones were taken, the teeth were extracted, and a small hollow needle was inserted into the sockets. Through this lipiodol was injected, and the specimen was examined by X-rays (fig. 1).

On examination the various radiographs suggested the following facts :—

(1) That the arteries to the teeth were not end vessels, and that along the upper border of the alveolus beneath the antral floor, and in the lateral antral wall, there are a series of anastomosing vessels, and that portion of the bone contains a vascular plexus (fig. 2).

(2) That it is possible by injection of one tooth-socket to inject the canals subservient to several teeth (fig. 5).

(3) That the canals to the central and lateral incisors run on the anterior wall of the superior maxilla (fig. 3).

(4) That the infra-orbital artery gives a series of descending vessels in an irregular and somewhat stellate manner (fig. 4).

(5) The lipiodol enters the antrum. On examination of the superior maxilla, it will be seen that the dental canals in the lower half of the bone become hemicanals in the upper part of their course. That is, they are grooves in the lateral antral wall, and the vessels which occupy them are sources of nutrition both to the teeth and the antral mucosa. They form in this region what may be called an antro-dental plexus (figs. 4, 5 and 6).

Microscopic sections of this region were prepared, and in the sections submitted some of the distal nerves and vessels are shown to be occupying this position (fig. 7).

The second specimen shows that these canals are less numerous after the teeth have been extracted, thus helping to prove that the lower half of these vessels are the true dental supply (fig. 8). If the superior maxilla be examined carefully from its alveolar aspect, it will be seen to be composed of spongy bone, and the tooth-sockets set amid a whole series of minute apertures. Doubtless in life many of these are filled with fibrous tissue and marrow, but the suggestion here entertained is that in addition to the anastomosis of vessels in the antral mucosa there is also an anastomosis in the bone. If this be so it will serve as an explanation why these teeth apparently do not show those changes which are so evident after a short time in those cases where they have been deprived of their blood supply.

FIG. 1.

FIG. 2.

FIG. 1.—Lipiodol injection of superior maxilla. Needles in position for the injection.
FIG. 2.—Injected superior maxilla to show the intercommunication between the tooth sockets. The lipiodol has travelled all along the alveolar region.

FIG. 3.—Injection of anterior tooth sockets. The lipiodol has travelled up into the infra-orbital canal.

FIG. 4.—Injection of anterior sockets. The network of canals subservient to the anterior teeth is clearly visible. The lipiodol has also entered the antrum.

FIG. 5.—Lipiodol injection of superior maxilla showing canals subservient to canine and incisor teeth. The posterior injection was made into the socket of the wisdom tooth. The network of vessels is well shown.

FIG. 6.

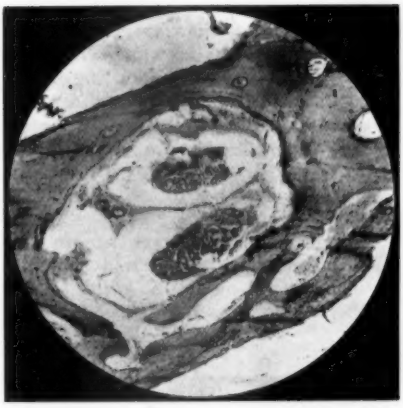

FIG. 7.

FIG. 6.—Injection of the posterior tooth sockets. Injection travelling along posterior superior dental canals.

FIG. 7.—Nerves running in the bony canals in the antral wall (outer wall).

FIG. 8.

FIG. 9.

FIG. 8.—Antral mucosa running into the canals in the bone.

FIG. 9.—Posterior superior dental nerve. The antral wall and mucosa (ciliated).

A series of sections of the outer bony wall of the antrum were taken, decalcified and stained. The antral mucosa was left *in situ*. On examinations of the specimens the following facts were suggested :—

(1) That at the lower border of the outer antral wall there are a series of anastomosing vessels which communicate very freely with one another. These are in the supra-alveolar region (fig. 7).

(2) The antral submucosa dips at intervals into the bony wall, and there again vessels anastomose (fig. 8).

(3) These vessels are probably subservient to the teeth, as after the teeth have been removed, they apparently disappear.

(4) The size of these vessels is such that a collateral circulation could be established more than sufficient to keep a tooth alive.

(5) The dental nerves run in bundles and do not ramify in with the vessels. There appears to be a vascular plexus, not a nervous one (fig. 9).

The tooth pulp.—A youth, aged 18, suffering from antral suppuration was subjected to radical antrotomy. At frequent intervals after the operation his

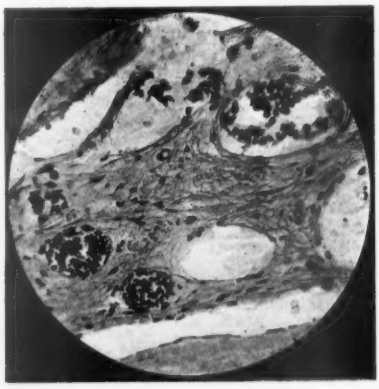

FIG. 10.

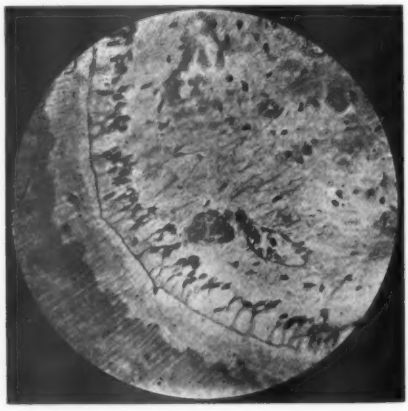

FIG. 11.

FIG. 10.—Blood-vessels of the tooth pulp.

FIG. 11.—The dentine and the odontoblast layer of the pulp (same pulp).

teeth were examined and the two upper premolars were found to be anæsthetic. This case was carefully watched and at the end of six weeks there was no change in the gum which was not retracted, and the teeth showed no other sign or symptom except that they were insensitive. With the patient's permission, for purely experimental reasons, one of these teeth was extracted; the socket bled freely. The tooth was placed in formalin and after fixation the dentine and enamel were ground down until the pulp chamber walls were about one millimetre thick. The specimen was then decalcified and after embedding in paraffin serial transverse sections were cut and stained. The examination of these showed :—

(1) Normal blood-vessels containing corpuscles (fig. 10). (2) Normal pulp matrix (fig. 11). (3) Normal layer of odontoblasts (fig. 11).

From a systematic search of the sections it was impossible to find any areas of degeneration, with the single exception of a few nerve filaments, which were known to have been cut.

From the appearance of this pulp I put forward the suggestion that the operation of radical antrotomy denervates one or two teeth, but the pulp still retains its vascular supply, and from careful scrutiny of thirty-three cases it appears to me that these teeth are no more liable to dental disease than are their neighbours, whose nerve supply has been retained. It is conceivable that when caries attacks these teeth, its progress will be more insidious than in a normal tooth, as the patient's attention is not drawn to it by pain.

Most of the operations of this series have been carried out by the President, by whose permission and help this paper has been prepared.

The radiography has been carried out by Dr. Harold Black, the section-cutting and staining by the Pathological Department of the University, and the photography by the Department of Physiology of the Birmingham University.

Discussion.—The PRESIDENT said that Mr. Strong's interesting piece of research, though limited to a small area, was complete in itself. He had conclusively shown that teeth known to be insensitive were not dead, but remained living.

F. N. DOUBLEDAY said he was sure that to those members of the Section of Odontology who happened to be present, the paper would prove very interesting. He thought that, in the main, it confirmed the textbook description of the blood and nerve supply of the antrum. In the Gordon Museum at Guy's Hospital there were beautiful specimens in wax, illustrating these points—made by John Towne, in the early part of the nineteenth century. The histological sections brought out two points. From the dental standpoint one would have thought that as much degeneration had taken place in that pulp as was likely in a patient of that age before the tooth was removed. The paper brought out the connexion of the blood supply and the lymph spaces of the antrum and the teeth, and indicated how easily infection might pass from the tooth or periodontal membrane through to the antrum, or in the reverse direction.

W. STUART-LOW said that this was an important piece of research. He (the speaker) had always thoroughly removed the lining of the antrum. If there were polypi they could be cleared out thoroughly with the lining from which they grew, otherwise there would be recurrence. Mr. Strong's research had shown that this could be done with impunity.

W. ARCHER HODGSON asked whether the fact that the tooth had lost its nerve-supply increased the risk of the pulp degenerating, and becoming infected eventually.

CECIL STRONG (in reply) said that the first question he set himself to answer was: Was there any blood supply to the tooth? The answer to that was Yes. The next question was: Was that blood supply sufficient to keep the tooth alive? The answer to that was Yes also. Then came the factor of the nerve supply. Whether there was any effect in that respect he did not know.

His remarks did not include Denker's operation. He did not know whether the operation caused the pulp to degenerate. He was not a firm believer in the trophic impulses; he thought they originated in limbs which had become denervated, and became to some extent degenerated. That was the degeneration of disuse. What was the use of the fifth nerve if the odontoblast was the receptor for the fifth nerve? He doubted whether section of the nerve, with the vascular supply left as it was, would cause the pulp to degenerate. He could not, however, answer that; he would have to examine more pulps some years afterwards.

Another point concerned the operation on the gasserian ganglion. Cutting the posterior root of the fifth nerve denervated sixteen teeth. A neurological surgeon told him he had never noticed changes in the teeth after that operation, though he had watched these cases for five or six years afterwards. Those teeth were denervated by cutting the peripheral axon, just as much as teeth were denervated by cutting the nerve immediately above the apex. He (the speaker) would extract a tooth from a patient who had undergone a gasserian ganglion operation, and see the result.

CASES

Atrophic Rhinitis treated by Cartilage Grafts.—W. A. MILL.

Female, aged 20, first seen in September 1931. For at least five years she had suffered from nasal obstruction, crusting, and ozæna. The condition present was advanced atrophic rhinitis, worse on the right side than on the left, to which side the septum was deflected. X-rays showed cloudiness of the right sphenoid.

September 5, 1932.—A large piece of cartilage was removed from the septum and replaced to narrow the right side of the nose. The right sphenoid was opened up.

April 24, 1933.—A piece of rib cartilage was introduced beneath the floor of each nasal fossa and adhesions were encouraged by excoriating the mucous membrane of the septum and the inferior turbinals.

January 16, 1934.—There was no ozæna, breathing was free, and although the patient had not used a douche for two months, there was only one very small crust in the right side.

Discussion.—HAROLD BARWELL asked what was done with the large piece of cartilage removed from the septum and replaced on September 5: where was it put? He had not had any experience of cartilage grafting, but some years ago he did a good deal of paraffin injection in cases of this kind, and, on the whole, he was disappointed with the results, as it was difficult to keep the paraffin in place; the mucous membrane was atrophic, and the paraffin came out again. There was improvement for only a short time.

DAN MCKENZIE said the great difficulty in Lautenschläger's operation was to get the lateral wall to remain adherent to the septum. It would adhere for some time after the operation was done. But later on the adhesions broke down and the patient became as bad as ever.

T. B. JOBSON said that cases of this kind were now seldom seen; the last two cases of his own he had treated with zinc ionization, and with very gratifying results, better than those obtained by any other method that he had adopted.

W. A. MILL (in reply) said that the septum was deflected, and he had separated the mucous membrane on either side, removed a large piece of cartilage, and turned it so that the convexity was towards the roomier side. He then eased it down so that there was a double layer of cartilage in the septum, to make it thicker.

Tuberculous Laryngitis; Pulmonary Tuberculosis; Syphilitic Aortitis; ? Aneurysm of Innominate Artery; Heart Block.—MAURICE SORSBY.

Patient, male, aged 53, was quite well until September 1933, when he developed a husky voice.

Present condition.—Slight cough and brings up a little sputum, which is blood-stained at times. Dyspnœa. Oscillating temperature (98° to 100°).

Examination.—Teeth bad. Lungs: a few crepitations at apex and base (right). Heart: deviated to left side; not enlarged. Larynx: right arytenoid much enlarged. Posterior end of right vocal cord thickened. Heaping up of greyish masses underneath the cords more marked on the left. Electrocardiogram: Heart block. X-ray examination: Syphilitic aortitis, ? aneurysm of innominate artery. Bacteriological report: Koch's bacillus present in sputum. Wassermann reaction + +.

HAROLD BARWELL said this patient had been proved to have tuberculosis and syphilis in the body, and the question was which of those diseases was affecting the larynx, or whether both were. From the appearance he thought the condition was syphilitic, especially in view of the thickened pachydermatous aspect of the vocal processes and the cartilaginous glottis. It was true that there was swelling of the arytenoid, but that occurred in syphilis as well as in tubercle.

Multiple Nasal Perforations.—M. L. FORMBY.

Male, aged 28. For the past eight weeks he has had a small round perforation in the left lateral wall of the nose. About three months previously he had noticed a swelling which slowly increased in size, became painful, burst, and left a hole in the nose.

There is a large perforation in the nasal septum. For four or five years there has been a discharge of crusts from the nose. The blood Wassermann reaction has been negative on two occasions.

Discussion.—HAROLD BARWELL said the patient was a glass mixer, who had to stir up powders which contained a powerful alkali and, sometimes, arsenic. It appeared that many people in the factory had sore noses. Hence this might be an occupational disease of the nose, allied to the better known ulceration caused by chromic acid.

DAN MCKENZIE referred to the case of a young woman who came to hospital with a perforation through the nasal septum. It occurred to him that this was likely to be something more than simple perforation, as it involved so much of the cartilage, most of which had disappeared. The patient's work was to pack table-salt for exportation. He visited the factory where she worked and went into the packing room. The air of the room was thick with particles of salt, which gave the appearance of a fog. Two-thirds of those working in that room he found had perforations of the septum. A report was made to the Factory Inspector, and a proper means of disposing of the salt dust was devised.

HERBERT TILLEY said the only case which he had seen somewhat similar to this was in an elderly man who had a rodent ulcer which commenced to grow on the septal nasal mucous membrane opposite the right middle turbinal. He (the speaker) removed most of the growth and the pathologist pronounced it to be rodent ulcer. Eventually it ulcerated through the skin over the inner half of the right nasal bone. Shortly afterwards the patient took his own life. The present patient's work did not expose him to chromic acid fumes. People who worked in irritating chemical atmospheres were liable to ulceration and perforation of the nasal structures, especially of the cartilage of the septum.

M. L. FORMBY (in reply) said he had had a provocative Wassermann test made, and the reaction was negative. After what Dr. McKenzie had said, he would inquire more minutely into the patient's occupation. It was important to ascertain whether any of the other factory workers were similarly affected. He did not think the perforation in the septum was syphilitic; it was his effort to correlate the two things that made him think of syphilis.

Epithelioma of Tonsil and adjoining Region of Tongue removed by Diathermy.—DAN MCKENZIE.

Male, aged 54. First seen April 1933. Epithelioma involving entire tonsillar area on the right side, with adjoining faucial pillars, soft palate, and tongue, of six months' duration. Ligature of external carotid and removal of glands on right side of neck, May 29, 1933. Entire pharyngeal growth including segment of tongue removed by diathermy knife, June 12. Pharyngeal wound healed, August 3.

Tumour of Tonsil and Soft Palate with Enlarged Glands in the Neck.—G. H. LAWSON WHALE, F.R.C.S.

Male, aged 47. Until the middle of October, 1933, he was doing a full day's work as a lighterman. The clinical appearance and history of the massive growth on the left tonsil, and the large bilateral glandular enlargements, suggest sarcoma, but the microscopic diagnosis is squamous-celled carcinoma.

Discussion.—LIONEL COLLEDGE said that Dr. McKenzie had obtained a very successful result, but it did not come within the accepted rule as to period of freedom from recurrence, because the operation took place only about ten months ago. A further eighteen months should pass before judgment could be passed. He suspected that an equally good result without deformity or scarring might be attained by using radium seeds. His own feeling about the treatment of large growths by diathermy had been that the results from it were less likely to be permanent than after irradiation treatment.

NORMAN PATTERSON, referring to the relative length of immunity from recurrence of these growths after diathermy on one hand, and irradiation on the other, said he did not think irradiation had been a recognized treatment long enough to enable definite conclusions to be formed on this point. He had been disappointed with the results of radium treatment, and therefore he had gone back to diathermy. He advocated the use of post-operative deep X-ray therapy. Sometimes in these operations he tied the external carotid; much depended on the extent of the growth and its situation. He did not consider Mr. Whale's case suitable for any form of treatment.

A. J. WRIGHT agreed that, wherever possible, diathermy should be used, as it was preferable to radium in this class of case. There was the great advantage that one still had irradiation in reserve if necessary. For Mr. Whale's case it would be as good as anything else.

HERBERT TILLEY agreed with those who favoured diathermy for this type of case, i.e. when the growth had spread superficially rather than infiltrated deeply into the normal tissues. Dr. Dan McKenzie would remember a case of an adult male in which he had helped the speaker. The patient was an adult male with a primary epithelioma of the left tonsil which invaded the neighbouring region of the soft palate and the upper region of the corresponding lingual tonsil. The infected regions were freely removed with a fine diathermy knife. The patient lived for seven years and died from pneumonia without any local recurrence of the epithelioma.

J. A. GIBB said there was an interesting question as to the lymphatic connexion between the tonsil and the mandible. Two years ago he had dealt with a case by exactly the method which Dr. McKenzie had employed in this case, and immediately after the operation he had inserted radon tubes. Three months ago the patient had come to hospital having carcinoma of the mandible. Three years ago he (the speaker) had had a case of carcinoma of the tongue and of the tonsil on the same side, which, again, he had treated by diathermy and radium, and there was, as yet, no sign of recurrence. He had treated thirty cases in a similar manner.

RITCHIE RODGER said that he had had a case in which he demonstrated the value of the two methods of treatment in the same patient. Nearly two years ago a man presented himself with a small sessile growth on the left anterior pillar of the fauces, and a specimen taken from it was found to be carcinoma. On the other side was a beautifully soft scar, perfectly healed, the site of a similar ulcer treated by diathermy five years before. The patient said that the pain after the previous operation had been so bad that he did not want the same treatment repeated. At his request, therefore, he (Mr. Rodger) tried radium, but it was of no use; the ulcer grew larger, and the patient died, having persistently refused to have treatment by diathermy.

W. J. HARRISON said he was glad to see evidence that the pendulum of treatment in these cases was now swinging towards diathermy. For growths in the soft palate and fauces his experience was that diathermy was infinitely better than radium. He could show one patient who had a growth which extended from the fauces and tonsillar fossa beyond the middle line of the soft palate and on to the hard palate. It was more than ten years since he was operated upon, and it was now possible to look straight into the Eustachian tubes, but the patient was quite well and fit. He was sure radium would not have produced that result. Another case was that of an aged clergyman who had an extensive growth on the cheek, which extended down on to his lower jaw. He died seven years later from a prostatic growth, but he had had no recurrence in the mouth.

T. A. CLARKE said that radium was particularly useful in tonsil cases; in those cases he had been disappointed by diathermy treatment. Among his own tonsil cases the longest period of freedom from recurrence after radium treatment was four and a half years; after diathermy freedom from recurrence was a matter of months.

BEDFORD RUSSELL said that during the last fifteen years he had examined every case of malignant growth in the upper respiratory tract and mouth at St. Bartholomew's Hospital treated by radium, diathermy or X-rays, of which 270 had been treated by radium, about the same number by X-rays, and many by surgery and diathermy. The conclusion was that the palate and floor of the mouth were favourable sites for such growths, whether treated by diathermy, X-rays or radium. Dr. Levitt always hoped to drive away a carcinoma of the palate with deep X-rays; his results were very satisfactory. In the tonsil he (the speaker) had been uniformly unlucky with radium. There were cases of growth in the tonsil treated by diathermy in which the patients had lived for three years after radium treatment, but in nearly all those cases, whatever the treatment, there was a recurrence in the glands. In cases of growth in the upper jaw he had not been successful (though two patients had been alive two years after treatment with X-rays). He and his colleagues had come to the conclusion that, in fairness to the patient, all three means should be used in every possible case. The best results were those in which the irradiated area was removed by diathermy afterwards.

The PRESIDENT said he was much interested to see how, almost universally, radium was now ceasing to be used in the treatment of these cases. At the General Hospital, Birmingham, however, there was a separate radium clinic for throat cases, and there were many patients attending it. He, personally, had been better satisfied with the results of radium treatment than with those of diathermy. Cases had been cured by diathermy, but the results of radium in the mouth, if properly applied, were very good indeed. Mr. Bedford Russell had said that radium was apt not to be satisfactory for growths of the tonsil and adjacent parts of the mouth; he (the speaker) thought a reason for that was a fear of putting the radium in sufficient quantity near the ascending ramus of the jaw. Hence the deeper parts of the growth were untouched, or insufficient radium was applied, or possibly it was not applied for an adequate length of time. At this clinic, therefore, the ascending ramus of the upper jaw—including, if necessary, the temporo-maxillary joint—was excised where necessary, so as to obtain a barrage of radium from inside as well as outside. The glands were apt to give rise to trouble. The rule which he had made was that it was not safe only to treat the primary growth with radium; the patient must in every case be watched, and told to return as soon as he noticed enlargement of glands. A patient might remain free from a primary growth for months and have no glands palpable, then suddenly a mass of glands would appear in the neck, the mass being inoperable when first seen. A better rule was to carry out a block dissection of the glands in the neck, whether glands were palpable or not. In Mr. Whale's case he (the President) would be inclined to attack the primary growth with radium, and the glands with a heavy collar of radium, or apply deep X-ray therapy, with the object of rendering the glands operable. On several occasions he had by this means rendered apparently inoperable glands operable. The opportunity of removing the glands by dissection must be taken when it occurred or the chance would be lost for ever.

DAN MCKENZIE (in reply) said he had had a number of cases of non-recurrence of cancer after diathermy removal. An old lady patient of his had an epithelioma of the soft palate, and after removal by diathermy had no recurrence and died of heart disease ten years after the operation. He had another still alive with no recurrence after eight years; in a third the growth had been removed by radium, then it recurred, and was removed by him by diathermy; this case showed no recurrence after seven years. Another had no recurrence after eight years, the growth in that case having been in the floor of the mouth. Another, in the tonsil was alive and well after four years. In not one of those was radium applied, the results were obtained by diathermic surgery alone. He was afraid of radium; he had seen its application followed by a rapidly increasing growth of the tumour. When a growth was anywhere in the palate or pharynx except on the tonsil, unless it was very advanced, removal by diathermy gave a good prospect of absence of growth for many years. But the chances of non-recurrence in epithelioma of the tonsil more particularly when it involved the tongue, as in the present case, were not good.

LAWSON WHALE (in reply) said he did not feel much clearer about the best procedure after the discussion than he had done before it, but he would adhere to the decision at which he had provisionally arrived before the discussion, namely, to apply, in the order named: (1) low tracheotomy; (2) diathermy; (3) a radium collar, and (4) block dissection of glands.

? Endolaryngeal Chondroma: Case for Diagnosis.—JOHN F. SIMPSON.

Male, aged 66. First seen in August 1932, when he complained of hoarseness for six months. Indirect laryngeal examination showed a smooth swelling of the left ventricular band. Both cords moved well. Wassermann reaction was negative. Radiological examination of chest and examination of sputum showed no evidence of tuberculosis. The nose showed chronic ethmoiditis and the antra were dark on transillumination. No glands felt in neck. Bilateral ethmoidectomy and double antrostomy performed and biopsy of the swollen ventricular band. The section showed no evidence of malignancy. The biopsy was repeated in September 1932 with same result. The swelling has slowly increased and in December 1933 a radiological examination of larynx showed a density in the situation of the swelling. At the same time marked irregularity of the anterior surfaces of the fifth and sixth cervical vertebral bodies was noted.

Discussion.—HERBERT TILLEY said that the growth was a remarkable tumour with a smooth potato-like surface, extending below the level of the cord. It should be examined through the direct tube, and probed so as to ascertain whether it was cartilage or growth. It did not affect the action of the vocal cord, and he suggested that it was either a fibroma or an enchondroma.

HAROLD BARWELL said that the point was whether the curious X-ray picture of the vertebral column had any connection with the laryngeal condition. It was a good principle not to diagnose two separate diseases at once; if the vertebral disease was tuberculous or syphilitic, probably the disease of the larynx was of the same nature.

J. F. SIMPSON (in reply) said he did not propose to do anything to his patient, who was able to carry on his work. If the growth now proved to be malignant after two years, it was too late to do very much for him.

Keratosis Pharyngis following removal of Tonsils.—CHARLES BENEY.

In August 1933 this patient, aged 24, had tonsillectomy performed on account of chronic sepsis, but no other pathological condition of the pharynx was noted before operation. Four weeks later the patient still complained of a slight sore throat on swallowing. White spots were seen at the base of the tongue and on the lymphoid tissue of the pharynx. This condition did not respond to local or general treatment. A recent pathological report by Dr. R. S. Ralph shows the condition to be keratosis.

HERBERT TILLEY said he did not think that the removal of the tonsil had had anything to do with the development of this condition. Years ago he himself had suffered from pharyngo-keratosis, although otherwise he was in perfect health. The condition caused a tickling in the throat, which produced violent attacks of spasmodic cough. This patient had white spots near the orifice of the left Eustachian tube and in the right pyriform fossa. He had not seen such deposits in the trachea, though he thought a case had been described by Chevalier Jackson. He himself had once removed a tonsil because it was so crowded with these keratinous growths as to produce much soreness. No treatment seemed to influence them, they appeared without apparent cause, and disappeared in due course with or without any treatment.

Section of Obstetrics and Gynæcology

President—W. Blair-Bell, F.C.O.G.

[*February* 16, 1934]

Post-menopausal Uterine Hæmorrhage

By V. B. Green-Armytage, M.D., F.C.O.G., F.R.C.P.

My first real interest in post-menopausal bleeding began after a visit to Nepal in 1924. I was summoned to see a woman aged 46, who had been bleeding excessively after a period of ten months amenorrhœa. The clinical diagnosis was that of fibroids, but when I saw the patient the local condition did not fit in with this and I was inclined to think that a malignant ovarian tumour had invaded the pelvic peritoneum. At operation, a tumour of the left ovary was removed, but it was impossible to deal with the right ovary, as it was involving the whole lateral wall of the pelvis.

Healing was uneventful and the patient was then treated by deep X-rays. Six years later I was requested to be present while Sir Frank Connor removed the gall-bladder, so that I might examine the pelvis thoroughly through the abdominal incision. This I did, but there was no sign or feeling of any growth whatever in the pelvis. Multiple sections were made of the ovary (which I had removed) in India, England and America, and the general consensus was that it was malignant, but I am inclined to think now that it was an innocent granulosa-celled tumour of the ovary.

Since then I have kept a methodical note of all cases of post-menopausal bleeding that have passed through my hands, both here and in Calcutta, dividing them, from a clinical point of view, into those that were due to visible or invisible causes. The visible speak for themselves and are shown in Table I as follows :—

Table I.—Visible Causes of Post-menopausal Bleeding.

Urethral caruncle (simple)	7
Urethral carcinoma	4
Vulval cancer	10
Decubital ulceration with prolapse	30
Traumatic ulceration due to pessaries, etc.	18
Granuloma pudendum	8
Tubercular ulceration of the vagina	2
Syphilomata and/or elephantiasis	5
Vaginal carcinoma	5
Vaginal polyposis	1
Polypi of the cervix (simple)	23
Inflammatory granulomata of the cervix	1
Cancer of the cervix (primary)	23
,, ,, ,, (after subtotal hysterectomy)	2
Tuberculous ulceration of the cervix	1
	140

One feature of this list which may excite comment is the comparative paucity of cases of cancer of the cervix. The reason for this seeming anomaly is that among the indigenous people of the tropics, maturity and child-bearing are almost synchronous events in the hospital class of patient. Indeed, among such people—since, from a religious and ethnic point of view, multiparity is the rule rather than the exception—I would go so far as to say that post-menopausal cancer of the cervix is very rare. To check this statement, in 1930—with the help of my registrar—I went through the out-patients' and in-patients' list for five years and found that out of 158 cases of cervical cancer, only 26 were in an operable stage when seen and only 15 had passed the change of life; of these, 9 were Europeans.

I have taken the menopause as a standard to mean the period of six full months after the cessation of normal catamenia.

Amongst pure Europeans, whether immigrant or domiciled, post-menopausal cancer of the cervix is not commonly seen, the reason in the former being that the wives of Europeans return to England with their husbands at about the age of 50, whereas in the case of the latter, habits of greater cleanliness as regards the genita tract and body are more universally practised in the East than they are in the West.

TABLE II.—INVISIBLE CAUSES OF POST-MENOPAUSAL BLEEDING.

Carcinoma of the corpus uteri	21
Sarcoma uteri	7
Fibromyomata and submucous fibroids	25
Polypi	37
Senile metropathia	7
Metropathia hæmorrhagica	17
Ovarian tumours (benign)	6
" " (malignant and primary)	34
" " (malignant and secondary)	2
Arteriosclerosis (hyperpiesis)	2
Granulosa tumours...	5
Tuberculosis (miliary) of uterus and adnexa	1
	164

This table is, to my mind, by far the more interesting of the two, in that it comprises not only cases in which an obvious tumour was palpable but also those in which doubt arose as to the probable cause and site of the bleeding, since in many of them nothing abnormal was palpable. In some the mucous membrane was grossly thickened and of the typical "Swiss cheese" pattern on section and, as expected, one could palpate the typical cystic enlargement of the ovary so well described by Wilfred Shaw and others, but in other cases one failed completely to do so.

In some the mucous membrane was perfectly smooth and atrophic, nothing coming away with the curette, and the uterus being small and thin. In others, perhaps many years after the menopause, one has suddenly found a hyperplasic mucous membrane accompanied by one small single polypus at the fundus, no larger than a pea.

Why do these patients develop symptoms of bleeding or conditions of inexplicable hypertrophy of the mucous membrane, perhaps so long as from ten to fifteen years after the change of life?

To my mind, since it has been recently demonstrated that the urine of 60% of women after the menopause contains prolan, the explanation of such bleeding must be sought in the anterior pituitary body, for how otherwise can we account for this Rip-Van-Winkle-like awakening of ovarian function?

Jeffcoate and Fluhman have suggested that the hypertrophy of the anterior pituitary, found at autopsy after the climacteric, is a compensatory readjustment of balance, following the gradual decrease of ovarian activity, the purpose of this revival of secretion being to stimulate the activity of the failing ovary. In favour of this view is the experiment of Zondek, in which he stimulated and obtained follicular response in the ovaries of female rats and mice by transplanting into them hypophyseal grafts.

The problem is one of intense interest, and will not be solved until the uterus and ovaries of every case of post-menopausal bleeding without palpable cause can be placed, immediately after operation, in the hands of the biochemist for analysis and animal experimentation, because at present we are in the dark as to whether this positive prolan urine reaction is due to inability of the ovary to utilize it or to a lowered renal threshold for its excretion.

Moreover, is it not possible that gynæcologists can or could advance the work of the biochemist by trying the effect of experimental transplantation into women and animals of grafts taken from the ovaries or endometrium of such a case?

In the table are seven cases of what I have called "senile metropathia" in opposition to the more general term "senile endometritis." My reason is that in none of them was there the least macroscopic or microscopic evidence of any inflammatory condition in the uterus, nor could I detect any pathological state of the ovaries. I have here a specimen, removed recently by vaginal hysterectomy on account of bleeding, from a patient aged 56.

How is it possible to explain the undoubted fact that an organ like the uterus can, after a long, latent period, suddenly give rise to symptoms of bleeding without any ulcerative lesion of its mucosa? What sensitizes the mucous membrane of this uterus? What starts the clock of ovarian function re-ticking? Surely it must be the anterior pituitary.

Passing now to the subject of pelvic neoplasms, only a small proportion of those that are innocent cause bleeding, even though they are twisted or accompanied by inflammation. In the personal record of 547 cases of ovarian tumours which I published in 1931, 63 were in-patients past the menopause; and four of these with innocent growths, and 26 with malignant growths had symptoms of uterine hæmorrhage. Since then I have seen eight more malignant and two more innocent ovarian tumours giving rise to this symptom. One of these was secondary to carcinoma of the large intestine, probably by way of retrograde lymphatic permeation.

My large experience of ovarian tumours confirms me in the belief that, in any case of post-menopausal bleeding where there is the slightest enlargement of the ovary or even resistance in either cul, laparotomy is called for, even though the bleeding is slight and temporary, since a large percentage of these cases are malignant, or, if not actually malignant, belong to the type of folliculomata.

To what is the bleeding due? Why are 75% of malignant tumours of the ovary bilateral? Why do so many of these patients suffer from primary sterility? The explanation must lie outside the pelvis, its anatomy and its blood and lymph supply. Zondek, Blair-Bell and Susman have shown that malignant tumours and folliculomata of the ovary in some 18% of cases after the change of life give rise to a positive prolan reaction, and that removal of the neoplasm causes this reaction to cease. Is it possible that an ovarian tumour in such a woman may take on the function of the original tissue, just as after thyroidectomy for cancer, metastatic tumours function like the original thyroid? The solution lies in the words of Harvey: "Study and seek out the secrets of nature by way of experiment." This we can only do in co-operation with the biochemist, for at present we do not know whether the growth stimulates the hypophysis to increased activity, or whether the growth actually manufactures the hormone; or, still further, whether the increased

activity of the pituitary is the cause of the malignancy and bilateral tumour formation. This aspect of malignancy, even though only confined to the genital tract, calls urgently for team work in every big hospital, between the biochemist in his animal laboratory and the surgeon in his ward and theatre, since Table II demonstrates that the percentage of malignant causes of invisible post-menopausal bleeding in an experience of ten years was 39·6%, whereas the incidence of malignancy among the visible causes was 31·4%, i.e. out of 304 visible and invisible cases of post-climacteric hæmorrhage, the total incidence of malignancy works out at 35·8%, which is considerably less than that recorded by Fahmy from the Edinburgh School. Some explanation of this discrepancy is due to the fact that post-menopausal cancer of the cervix is rare in the East, for the reasons that I have given, although ante-menopausal cancer of the cervix is exceedingly common.

Of the five granulosa tumours, four were innocent; one only was definitely malignant on section (the patient died four months later from a metastases in the lung).

Treatment.—It is not my intention to deal individually with the laparotomy treatment of these patients, but I want to put in a strong plea for the vaginal-surgical—as against the radium—method of treatment in certain cases. In saying this, I feel somewhat like Daniel amongst the lions, for I fully appreciate that there are many here who, for cases of metropathia hæmorrhagica and the like, prefer the application of radium after curettage.

For my own part, in all cases of metropathia, and even where polypi and submucous fibroids occupy a post-menopausal uterus which is no bigger than a nine-weeks' pregnancy, I prefer to carry out vaginal hysterectomy, which can be done in under forty-five minutes, is almost a bloodless operation, and in 99% of the cases is followed by a painless convalescence with no post-operative disabilities. Moreover, I am not at all sure that it is not, in the long run, a cheaper method of treatment, as the patients are up and away between ten and fifteen days afterwards.

Up to date I have performed 329 vaginal hysterectomies with four deaths only, that is a mortality of 1·2%. In only one case (an early one) was the bladder injured. In none did secondary hæmorrhage occur.

I am aware that this operation is, with many, an unpopular one, but I am quite sure that it is the ideal operation for many of those cases of ante- and post-menopausal benign bleeding which occur in patients whose uteri, small or moderately large, are unaccompanied by adhesions of old, inflammatory, adnexal disease.

Radium, I know, has its advocates, but I consider that its disadvantages overweigh its advantages, since in some cases it fails to achieve its object, in others it gives rise to a constant discharge, causing pruritus, and in still others it manufactures in the mind of the woman and/or her relatives an obsession of cancerophobia, which many of us here have met and have been unable to counter.

Discussion.—Professor MILES PHILLIPS said that in preparing such an analysis as this, it was necessary to decide exactly when the post-menopausal era commenced. Mr. Green-Armytage allowed six months to elapse since the last menstrual loss. Dr. Fahmy in a similar analysis reported to the Birmingham Congress in 1933, allowed the more satisfactory period of one year. This might explain the surprisingly large proportion of cases in this series in which the bleeding was said to be due to uterine fibroids which rarely caused bleeding after the menopause was completed but not uncommonly did so during the epoch which might be called intra-menopausal.

On the other hand although cancer of the corpus uteri was most commonly (75%) post-menopausal, it was also not infrequently intra-menopausal and even ante-menopausal. He (Dr. Phillips) thought this subdivision helpful in reminding the medical attendant of all the possible causes of bleeding at this dangerous epoch in woman's life.

Professor BECKWITH WHITEHOUSE said that, in his opinion, some of these cases of post-menopausal uterine hæmorrhage were not associated with any local lesion in the uterus but were really related to delayed ovulation. He had seen a uterus and ovaries—removed from a patient in the sixth decade on account of uterine bleeding—in which one of the ovaries contained two cystic graafian follicles and also a small but recent corpus luteum. It should be recognized that cases of Schröder's disease occasionally caused symptoms after the menopause.

He was interested in the high proportion of cases of simple adenomatous polypi in Mr. Green-Armytage's series and suggested that the growth of these small polypi could be explained upon a simple mechanical basis. They always appeared to grow where the walls of the uterus were not in contact, in other words, where there was a local lowering of intra-uterine tension. He did not think that it was always necessary to invoke the stimulus of hormonic action, especially in cases where endometrial hyperplasia was localized.

Mr. GREEN-ARMYTAGE (in reply) said that he laid particular emphasis on a period of six months' amenorrhœa before the onset of irregular bleeding in the menopause for the specific reason that many cases of cancer of the cervix, etc., were missed because practitioners, thinking this bleeding was normal, failed to examine their patients efficiently. For this reason, although twelve months was perhaps the best physiological time limit, from the point of view of patient and practitioner, he considered it advisable to adhere to a six months' limit.

Professor Whitehouse had remarked on the number of fibroids and submucous fibroids as the cause of post-menopausal bleeding, but as two-thirds of these cases were met with in the tropics, he would appreciate the fact that Howard Kelly, himself (the speaker) and others had observed the greater frequency of these tumours in hot countries and coloured races.

Vaginal Hysterectomy

By MORRIS DATNOW, F.R.C.S.E.

Introduction.—The advent of radium in the treatment of uterine cancer has diminished the number of hysterectomies performed; an advance in our knowledge of the hormones will make a still further reduction. There will, however, always remain a certain number of indications for extirpation of the uterus.

In some clinics vaginal hysterectomy is not performed at all, in others, very rarely. So one should perhaps apologize for expressing one's belief in the value of this operation. It is not merely enthusiasm on my part, but is my real conviction that there are circumstances which call for removal of the womb by the vaginal route in gynæcological—and occasionally in obstetrical— practice, just as there are times when it is best to adopt the abdominal method of approach. In order to procure the best results for his patients, the gynæcologist should not dogmatically follow definite procedures to the exclusion of all others. He should be capable of resorting to every method of treatment and have them all at his command. A judicious selection of methods and material is the ideal to strive for.

It is my purpose to point out the indications for vaginal hysterectomy, and to refer to various details in the technique which have helped to facilitate the procedure.

Historical note.—A review of the development of the operation of vaginal hysterectomy shows that the present technique, at any rate, originated from attempts that were first made to cure cervical cancer. Simple cauterization was originally practised, later, amputation, and finally, vaginal hysterectomy. Sauter is said to have performed the first successful vaginal hysterectomy in 1822, Blundell in 1828, and Recamier in 1829. Many failures were encountered

subsequent to these, probably as the result of imperfect asepsis and the lack of anæsthetics.

Only a few cases are found in the literature after this until Freund in 1878 described his method of performing the operation, and it is from this that the present-day technique has developed.

Czerny watched Freund operating and in his article "Uber die Ausrotting des Gebarmutterkrebs," described an improved Freund's technique; to him the credit is due for again popularizing the operation. His first operation was performed, August 12, 1878, for carcinoma of the cervix. It took two hours and the patient finally ended up with a fistula. Silk ligatures were used. The convalescence was stormy, and the patient died January 19, 1879, five months after the operation, from what appears to have been an ascending infection of the urinary tract.

Four vaginal hysterectomies for cervical cancer are described in his series of articles, in all of which the patients eventually died.

From 1879 onwards vaginal hysterectomy became an established procedure, and alterations, additions, and modifications were continually being discussed. The operation did not rapidly become popular and six years later—i.e. as recently as 1885—Duncan wrote: "Extirpation of the entire uterus being an operation still *sub judice*, it becomes the duty of everyone who has performed it to publish the result whether favourable or not." He described two cases at great length.

Up to the present century most authors only describe sporadic cases and no large series is to be found.

Liebman, Hegar, Kaltenbach and Martin all played an important part in developing the earlier technique. In the present century, Kelly, Schuchardt, Schauta, Adler and their school are the main exponents.

Advantages of vaginal hysterectomy over abdominal hysterectomy.—I do not wish to create the impression that vaginal hysterectomy should be the routine procedure for removal of the uterus, but rather to emphasize that where a choice can be made between this and abdominal hysterectomy, the scales should be allowed to weigh on the side of the vaginal route for the following reasons:—

(1) There is less shock.
(2) There is a more rapid convalescence, and the patient's stay in hospital is shortened.
(3) There is better drainage.
(4) The absence of a scar has a psychological effect upon the patient, and many will more readily submit to operation when informed that their abdomen will not be opened.
(5) There is no risk of incisional hernia.
(6) A prolapse operation can be combined with the hysterectomy and thus save the necessity for a double procedure.
(7) Post-operative care of vaginal hysterectomy patients is simple.

Contra-indications to vaginal hysterectomy.—The only drawbacks to the removal of a uterus per vaginam are dimension and fixity. The optimum size will depend upon the experience and dexterity of the operator, and has been variously stated to be between that corresponding to an eight-weeks' pregnancy and a full-term fœtal head. The larger the uterus, the more difficult will be the extirpation, the limit being given by Professor Miles Phillips as corresponding to a full-term fœtal head.

If the uterus is fixed either by old inflammation or by a previous operation—such as a ventral fixation—vaginal hysterectomy becomes a most difficult and dangerous operation, and sometimes even has to be abandoned.

It is better to treat carcinoma of the body by abdominal hysterectomy, as by this method the uterus is handled less. Further, malignant disease of the body tends to occur more frequently in nulliparous women in whom the vaginal operation is, of

course, rather more difficult to carry out. Lastly there is a group of cases in which it is desired to explore the other abdominal viscera. Here, naturally, the abdominal route is to be favoured.

Indications for vaginal hysterectomy.—As already pointed out, the indications for vaginal hysterectomy are rather elastic and relative. The choice of cases should have regard to the advantages of the vaginal route over the abdominal, and the contra-indications should be borne in mind. Apart from this there can only be the personal element. As far as the patient is concerned, there can be no question that vaginal hysterectomy is to be preferred whenever it can be carried out, and below are set out the circumstances under which it should be possible to accomplish the operation:—

(1) "Bleeding uterus"—caused by (*a*) multiple small fibroids, (*b*) chronic subinvolution with a badly lacerated precancerous cervix and frequently accompanied by cystic ovaries, and (*c*) polypi in the fundus and not within reach—at about, or after, the menopause, especially when there is an associated prolapse as so often happens, which is causing symptoms and requires attention.

(2) When a hysterectomy is indicated in a very stout woman, it will be found simpler to perform it from below, provided that the uterus is not too large or fixed.

(3) If it becomes necessary to perform hysterectomy in the presence of skin disease of the abdomen, burns (following hot applications), or when a colostomy is present.

(4) A septic uterus after criminal abortion should be removed per vaginam when the surgeon does not suspect an injury to any of the other viscera.

(5) An inversion of the uterus.

(6) It is better not to open the abdomen when there is any cardiac or respiratory disease present and a hysterectomy is indicated.

(7) For radical treatment of carcinoma of the vagina.

(8) For radical treatment of carcinoma of the cervix.

(9) For incomplete treatment of carcinoma of the cervix, preliminary to some complimentary treatment, such as lead therapy.

(10) For carcinoma of the body of the uterus in certain cases and with special precautions. Several authors favour this route for this disease. One should, however, bear in mind that the uterus is handled a good deal during its removal through the vagina. Preliminarily to removing the uterus the cervix should be firmly closed by means of sutures.

Stages in the operation of vaginal hysterectomy.—The steps employed during vaginal extirpation vary slightly in different clinics; they are so well known that detailed description would be superfluous. It will therefore be sufficient simply to enumerate the stages and append any points which have been found to simplify the procedures.

The three main methods of approach for vaginal hysterectomy are:—

(1) "From the uterus," i.e. the fundus is first delivered and ligation of the vessels is commenced from above.

(2) By splitting the uterus and then removing each half separately.

(3) From the broad ligaments, which is the method we employ, and is referred to below.

The steps in the operation are:—

(1) Incision: better hæmostasis is obtained if the incision is made before going on to (2).

(2) Closure of cervix and insertion of silk cervical tractors; this procedure diminishes the number of instruments in the vagina, and prevents any uterine contents from escaping.

(3) Division and ligation of the cervical branches of the uterine vessels.

(4) Incision of the pouch of Douglas and insertion of a gauze pack to keep the abdominal contents out of the way. It is advisable at this stage to insert the finger—in order to feel for the presence of any adhesions—and to survey the position.

(5) Incision of the utero-vesical peritoneum and insertion of a gauze pack. Here the finger is again passed round in front of the uterus. This step in the operation is facilitated by not making the anterior incision on the cervix too deep, and pushing the bladder well up by means of gauze dissection. It also helps if a strip of gauze is used as a plug to hold the bladder out of the way whilst the peritoneum is being incised.

(6) Division and ligation of the utero-sacral ligaments. It is essential to carry this out here, as it allows the uterus to come down and facilitates the next step.

(7) Division and ligation of the parametric tissue containing the uterine vessels on each side. It is a mistake to adhere to one method of carrying this out. We have found it useful to employ two procedures: (*a*) the clamp, cut, and ligature, and (*b*) the insertion of ligatures by means of a pedicle needle.

(8) Delivery of the fundus uteri through either the posterior or anterior incision, whichever is the simpler.

(9) Clamping and ligation of the infundibulo-pelvic ligaments, ovarian and round ligaments. This step is facilitated by employing a hook devised by Professor Blair-Bell.

(10) Closure of the peritoneum. The vessel stumps should be pulled down and stitched so that they are extra-peritoneal.

(11) Closure of vaginal incision.

(12) Insertion of iodoform gauze pack.

Post-operative treatment.—The after-care of the patients is simple. The bladder should be kept empty; all packs are removed twenty-four hours after the operation. Vaginal irrigations with 5% eusol through a No. 9 catheter are begun on the fifth day; no force should be used. The patient is allowed up on the tenth day.

If hæmorrhage should occur, the vagina is again packed, and if this is not sufficient to check the hæmorrhage, the bleeding point should be sought and ligated.

The table below gives an analysis of 196 cases in which vaginal hysterectomy had been carried out.

Disease	No.	Remarks
Carcinoma cervicis	26 ...	1 died soon after operation 5 alive and apparently well, 7 to 11 years 6 not traced 5 less than 5 years
Fibroids	45 ...	1 died a few minutes after completion of operation
Chronic metritis	5	
Chronic subinvolution	32	
Adenoma cervicis and other cervical lesions (non-malignant)	19 ...	1 with double pyosalpinx 1 with complete procidentia
Enlarged retroverted uterus ...	7	
Menopausal bleeding	12	
Precancerous cervix	14	
Metrostaxis	8	
Endometrioma of ovaries	1	
Pyometra	3	
Adenomyoma	1	
Cystic ovary with bleeding ...	4	
Complete prolapse	11 ...	1 included under fibroids as well
Uterine polyp	3	
Complete tear with prolapse ...	1	
Bilateral hydrosalpinx	1	
Vesico-vaginal fistula	1	
Pelvic infection	1	
Puerperal sepsis	1 ...	died 14 days after operation
Total ...	196	

67 had prolapse operations (including the 11 complete prolapse cases).

I am indebted to Professor W. Blair-Bell for allowing me to make use of his cases.

Discussion.—Mr. A. C. PALMER: A number of questions might fairly be asked in connexion with vaginal hysterectomy:—

(1) Why take the trouble to remove the uterus from below, when in the majority of cases it is an easy and simple procedure to remove it through an abdominal incision?

Most people agree that there are women whose abdominal subcutaneous tissue is so overburdened with fat, that the mere opening and closing of the abdomen is in itself something of an undertaking. I regard these cases as suitable for vaginal hysterectomy. It matters little whether the patient has or has not had children; in the latter case, all that is necessary is a variation in the earlier part of the operative technique. In nulliparous patients I usually begin the operation by the posterior—rather than the anterior—approach.

(2) is suggested by (1). Why impair the integrity of the abdomen by a fairly large incision into it when the uterus is already doing its best to come out below and its removal by this route offers an opportunity for radical cure of associated hernial protrusions? By these are meant, of course, cystocele, rectocele and hernia of the pouch of Douglas.

The answer to this question should be obvious.

(3) Is it a fact that women with prolapse sometimes complain of excessive or irregular bleeding?

In my experience they do, and in my series of cases there are 47 examples. I am in the habit of calling this condition of prolapse associated with bleeding, "the prolapse syndrome."

(4) Is it an advantage or a disadvantage to remove the uterus during repair operations?

It used to be said that the removal of the uterus deprived the operator of a fixation point for the vault of the vagina. In my experience, this is not the case. When the uterus is out of the way one can see the lateral pelvic and utero-sacral ligaments and more easily bring them into use as a support for the vault.

Another and, perhaps, even more important point is that, when the uterus is outside, the extent of the hernia of the pouch of Douglas can readily be explored and a radical cure more easily performed. I would almost go so far as to suggest that in the efficient radical cure of procidentia, preliminary vaginal hysterectomy is a necessary step.

(5) What kind of uterus is suitable for removal by the vaginal route?

First with regard to size: Any uterus which is not appreciably larger than a fœtal head. Secondly: A uterus the fundus of which is freely movable, that is to say, not fixed to ovarian cysts or tubes already adherent to the pelvis and so far as one can tell, not fixed to the gut. Thirdly: With regard to the pathological condition of the uterus? I would suggest that the bleeding is commonly due to fibroids or chronic subinvolution, less commonly, to carcinoma of the body. All three are equally suitable for vaginal hysterectomy, provided the two conditions mentioned above are met.

Professor MILES PHILLIPS said that he had been taught to use the vaginal route for removal of the uterus whenever practicable, and he had advocated it in public discussions on several occasions. It was, however, refreshing to hear, at last, its use urged as an aid in the operative cure of genital prolapse.

The obese and "poor subjects for operation" were best dealt with by the vaginal route; lighter anæsthesia was required, there was less shock, less pain and easier after-nursing than after the abdominal operation. Also, remote sequelæ, such as incisional hernia and intestinal obstruction from adhesions, had never occurred after the 660 vaginal hysterectomies he had personally performed. The association of genital prolapse with conditions requiring removal of the uterus was, in his opinion, the most common indication for this operation, which obviated the difficult procedure of colporrhaphy in a case in which a total hysterectomy had been previously performed. Again, not a few women greatly dreaded an abdominal section and were immensely relieved to hear they were not "to be cut open" and especially so if they were to get two operations—removal of a bleeding, painful or discharging uterus and relief from prolapse—at one sitting.

The chief reasons for removing the uterus when operating for genital prolapse were: (1) All the usual indications for hysterectomy—excluding gross enlargement of the uterus, and, of course, nowadays, cancer of the cervix—but including even early carcinoma of the corpus in the obese. (2) Certain conditions of the cervix which rendered it unsuitable for amputation, e.g. very deep lacerations, large ectropions especially if infected, diffuse cystic cervicitis, atrophy with stenosis of the canal especially if accompanied by atrophic pyometra.

Additional advantages gained by removing the uterus were: (1) Cure of an accompanying hernia of the pouch of Douglas (enterocele). (2) Cure of accompanying broad ligament or

ovarian varicoceles. Both these conditions might cause much discomfort and disappointment after an otherwise successful double colporrhaphy.

[Professor Phillips enumerated the following chief points in the technique of the prolapse operation :—

(1) In using the incision which Fothergill recommended in anterior colporrhaphy with removal of the cervix, the urethra and adjacent bladder should not be laid bare until the hysterectomy was completed, so avoiding troublesome oozing from the sinuses in that position.

(2) Clamp, cut, and ligate each vessel and pedicle in turn.

(3) Use hardened catgut only, to avoid sinuses.

(4) Open the peritoneal cavity through the pouch of Douglas first in most cases.

(5) Clamp and divide each utero-sacral fold, ligaturing and fixing each to the adjacent vaginal skin edge by a mattress suture of thick catgut. This should be *tied on the upper peritoneal surface*, in order that the long ends may, at the end of the operation, be left protruding into the upper vagina ; this ensures drainage from the potential space between the the closed peritoneum and the vaginal vault, and is a much more satisfactory method than the use of gauze or rubber.

(6) Between these place three or four mattress sutures—or a continuous suture—of fine gut, to sew the adjacent peritoneal and vaginal edges together, and so prevent otherwise troublesome bleeding.

(7) Push the bladder and adjacent (unseen) ureters off the supravaginal cervix very carefully and thoroughly—when necessary using a broad retractor to hold them out of the way whilst opening the utero-vesical pouch.

(8) It is often easier to remove the appendages, one or both as indicated, separately after the uterus has been cut away.

(9) If the ovaries are not removed, cut off the tubes or at least their uterine ends, to prevent them prolapsing into the vaginal vault, where the mucosa may proliferate into a growth of alarming character.

(10) It is rarely necessary to excise any excess of peritoneum of the enterocele—eventrate it by suturing the utero-vesical peritoneal edge as high up as possible on to the posterior wall of the pouch of Douglas. The excluded plaque of peritoneum usefully helps to fill up the space above the vaginal vault.

(11) Before closing the peritoneum recount the swabs and packs as in abdominal sections.

(12) Close the peritoneum completely with three or four mattress sutures of thin catgut —the lateral ones fixing the ovarian pedicles and round ligament stumps outside the peritoneal cavity.

(13) Holding up the bladder, ureters, and urethra on retractors of lessening size as the gap is closed, suture the paracolpos from side to side by means of buried mattress sutures of thick gut passed *parallel* to the vaginal edges, thereby diminishing the risk of pricking vessels or even the ureters. The first of these is passed through the utero-sacral folds.

(14) Suture the vaginal edges.

(15) The posterior colpo-perineorrhaphy. The operation might be a difficult one, especially if there was much scar tissue. Judgment was required in selecting cases, and it was occasionally judicious to leave a large posterior colporrhaphy to a second sitting if the operation had been unusually troublesome. Ward sisters considered that no operation earned greater gratitude.]

With regard to mortality, he (Dr. Phillips) thought that his own was too high : in 660 cases there had been 13 deaths—a trifle under 2%. This included all cases from as far back as 1908 onwards. The technique had been greatly improved in recent years. All his last 102 private cases had been successful.

During the discussion he had been reminded that he (1) occasionally found it advantageous to split the uterus vertically, and (2) often used the Trendelenburg position in order to keep the bowel away from the field of operation.

Professor BECKWITH WHITEHOUSE : I am glad that the Section has had the opportunity of discussing vaginal hysterectomy, because I feel that a valuable and useful operation in recent years has been somewhat neglected by British gynæcologists. Many, if not the majority, of our students to-day complete their training without ever having seen extirpation

of the uterus by the vaginal route. This was not so when I was a student thirty years ago and it is not so to-day in many continental clinics. Fraenkl of Vienna told me last year that he still regarded the vaginal operation as the method of choice and was surprised to find that in Britain and America abdominal hysterectomy is usually preferred to a method which, from the patient's point of view, has many things in its favour.

There is no doubt that radium therapy has largely supplanted hysterectomy in the treatment of uterine hæmorrhage and has removed one of the favourite indications for the vaginal operation of former days. At the same time there still remain an appreciable number of hard fibrotic and painful uteri which bleed from an atrophic endometrium and for the treatment of which radium is unsuitable. For some years it has been my practice to deal with this type of case by vaginal hysterectomy, and the results have been entirely satisfactory.

In my earlier cases I frequently experienced some difficulty in separation of the bladder and incision of the utero-vesical pouch of peritoneum, especially when the uterus was rather large and fixed, or when hypertrophy of the supravaginal cervix was present. Difficulty also occurred on occasion from troublesome venous bleeding from unsecured plexuses at the base of one or other broad ligament.

These troubles have been overcome in recent years since I adopted the technique described by Professor P. Werner of Vienna, an operation which I heartily recommend when no question of malignancy arises.

The essential feature of Werner's operation is bisection of the uterus in the middle line and removal of each half of the organ separately. A circular incision is made round the vaginal cervix through the vaginal wall. The bladder is separated and retracted. The cervix is then split anteriorly with scissors, as high as the vesical attachment, and the incision carried upwards until the anterior pouch of the peritoneum is opened. A retractor is introduced through the aperture in the peritoneum, and the uterine incision then carried up to the fundus. At this stage the body of the organ can usually be delivered, and the bisection is completed by carrying the incision from the fundus through the posterior wall to the pouch of Douglas, and the posterior lip of the cervix. Bleeding is negligible, as the mid-line of the uterus is relatively an anæmic field of operation. One half of the uterus may now be returned, if desired, to the peritoneal cavity. The other half is drawn down, and the round, infundibulo-pelvic and utero-sacral ligaments are successively divided between clamps. Finally, the uterine artery and veins are clamped and divided, and the half of the uterus with its corresponding appendage extirpated. The same procedure is carried out with the remaining half.

The cut peritoneal edge in front and behind is then sutured to the vaginal margin, and if any oozing remains a gauze drain is inserted. There is no necessity to close the vaginal incision.

I usually reserve this useful operation for cases having the indications already noted, but even when adherent inflammatory appendages are present, it is surprising how easily separation is effected by dissection from below.

Mr. GREEN-ARMYTAGE said that he had performed 329 vaginal hysterectomies with four deaths only—a mortality of 1·2%—and preferred this method for the majority of those cases of benign hæmorrhage which were in many clinics treated by radium, because radium sometimes failed and often caused pruritus and cancerophobial obsessions. From an administrative point of view, whether in hospital or in private practice, operation had the great advantage of being a cheaper procedure. In the matter of technique, he had gained considerable benefit, with regard to oozing, by adopting Danforth's advice to inject 1 c.c. of pituitrin into each paracervical plane before making any incision. If intestine tended to bulge through the utero-vesical pouch, he preferred to put the patient slightly in the Trendelenburg position rather than to insert a strip of gauze. He invariably used No. 1 catgut and had never seen secondary hæmorrhage. He had found this operation valuable in four cases of chorion epithelioma; bleeding was negligible, sepsis was avoided, drainage was excellent, and there was no shock—all great advantages where an anæmic patient was concerned.

Mr. W. W. KING said that he regarded vaginal hysterectomy as the operation of election when possible. He had performed 539 vaginal hysterectomies at the Jessop Hospital, with 12 deaths. Three of these deaths had been from uræmia; post-mortem examinations had

shown that the ureters had not been injured in any of the cases. Death was due to operating on bad renal risks without having had the N.-P.N. estimated. He had this estimation made now in all doubtful risks. Three patients had died from pulmonary embolus, two from peritonitis, one from obstruction, one from cardiac failure, and in two cases the notes did not record the cause of death. He did not agree with Mr. Green-Armytage's suggestion of lowering the upper part of the body while doing a vaginal hysterectomy, as to do this allowed infected material to run into the upper abdomen. He did not think that it was necessary to remove the tubes in every case; the procedure complicated the operation and was liable to interfere with the ovarian blood-supply. He had never had to remove a tube at a subsequent operation in this series, but had had to do so in a private case. He always removed the tubes and ovaries when operating for carcinoma of the uterus by this route.

JOINT DISCUSSION No. 2.

Section of Neurology, and Section of Therapeutics and Pharmacology

Chairman—S. A. KINNIER WILSON, M.D. (President of the Section of Neurology)

[*December* 21, 1933]

DISCUSSION ON THE TREATMENT OF SUBACUTE COMBINED DEGENERATION

Professor Edward Mellanby: I am reluctant to precede Dr. Carmichael in opening this discussion because the work I wish to describe is mainly of an experimental nature, and although it is difficult to avoid the conclusion that the results have some bearing on the ætiology and treatment of subacute combined degeneration of the cord, the evidence at present available is by no means conclusive. Indeed, the facts to be described may only add to the difficulty of the situation. However, there have been so many examples in recent years where experimental and clinical investigators have met together and discussed—with fruitful results—problems of disease, from what appear at first sight to be points of view with very little in common, that we can probably afford to be optimistic even on the present occasion.

Some essential points to be borne in mind in considering this disease are that it is a condition of nerve degeneration in the spinal cord and peripheral nerves, that the nerve changes are primarily those affecting the myelin sheaths, that the degenerative changes are unaccompanied by inflammatory reactions and with little or no neuroglial overgrowth, and that subacute combined degeneration is classed with pellagra, convulsive ergotism, and lathyrism, as toxic and not infective in character. If the spinal cord of a patient deceased of any of these diseases was presented to a pathologist for diagnosis, he would probably have some difficulty in deciding which was responsible for death.

A further point of fundamental importance is that all recent work has emphasized the fact that subacute combined degeneration of the cord is a metabolic disease. Its close association with pernicious anæmia—now controllable by liver and its water-soluble extracts or by desiccated pig's stomach,—and the general view, although there are still great differences of opinion as to the means of so doing, that these degenerative nerve changes can also be prevented and relieved, if present, by dietetic means, support the idea of a nutritional basis being involved.

If, in addition, it is possible by dietetic means to produce and prevent experimentally comparable lesions in the spinal cords and peripheral nerves of animals, involving demyelination of conducting nerves in the absence of inflammatory reaction and neuroglial overgrowth, it will be agreed that such an experimental basis may afford a means of adding valuable knowledge to the metabolic processes which underlie the disorder.

I wish, therefore, to give a bird's-eye view of evidence which demonstrates not only that the spinal cord is within the pale of nutritional influences, but also that the so-called toxic degeneration of the nervous system can be produced by certain ordinary foodstuffs and can be prevented by specific food ingredients; that, in other words, there are neurotoxic agents in food which can only act and hasten demyelinative changes in nerves in the absence from the diet and from the body of certain essential protective factors in food.

My attention was first attracted to this subject about ten years ago when I noticed that some of my experimental dogs in which I was studying the cause of rickets, developed severe inco-ordination of movement and other symptoms of

nervous disorder. After having decided that this condition was independent of rickets, I examined their nervous systems and found extensive myelin degeneration in certain parts of the spinal cord [1]. It became evident in course of time that there were two properties of the diet which produced these degenerative changes; (1) it contained much cereal, and (2) it was deficient in fat-soluble vitamins.

Cereal content of diet.—Whereas the nervous changes were evident when white flour formed the cereal factor of the food, they were increased when wheat germ or embryo was added. Since the behaviour of the dogs and the nerve degeneration in the cord reminded me of the clinical condition known as convulsive ergotism in man, it seemed possible that the wheat embryo which increased the morbid changes was ergotized, i.e. invaded by the mycelium, *Claviceps purpurea*. Microscopic examination did not support this possibility, but my attention having been drawn to ergotism, I proceeded to add ergot of rye to the diets and found that this increased the nerve degeneration. Rye germ not infected by the ergot mycelium also increased the cord changes. In fact, it became clear that all cereals tested (with one exception) under these particular experimental conditions, allowed demyelination of conducting nerves in the cord to develop, and that cereal embryo and especially ergotized rye germ made the condition worse. I assumed that cereal and especially cereal embryo and ergot contained a neurotoxin. The exception among cereals was yellow maize for a reason which will be obvious later. When yellow maize was eaten no degeneration was produced even when additional ergot was eaten. White maize, on the other hand, allowed these changes to develop [2].

Vitamin A and carotene as the protective factor.—It has been mentioned above that the cord changes only occurred when the diets were deficient in fat-soluble vitamins, and it became necessary to see which vitamin was capable of exerting this protective influence. At first this was a matter of some difficulty, as the earlier work was done before a clear differentiation between vitamins A and D had been made. With the preparation of pure vitamin D it was possible to add this singly to the diets, and it was then evident that this particular substance was not the protective factor. It was indeed found that ergot itself contained vitamin D, and it was unlikely that a substance which made the degenerative changes worse should contain a protective vitamin in any quantity. Thus while ergot prevented rickets in these young animals, it made the spinal cord degeneration more severe.

When attention was now turned to vitamin A, it soon became evident that this was the essential protective factor, for any source of this vitamin prevented the nerve degeneration. Thus butter, egg-yolk, mammalian liver or liver oil had a protective action. Green vegetables and carrots also had the same protective influence, and this led to the idea that carotene, in this as in other biological properties, acted like vitamin A. This was found to be the case, for the addition of 2 to 3 mgm. of carotene to the diet daily prevented the myelin degeneration even when ergot was present in the diet.

It is impossible here to discuss these experimental results or their significance in any detail, but reference may be made to a few more outstanding points.

(*a*) Of the two dietetic factors which form the basis of these results—a neurotoxic influence associated with cereals, and a protective fat-soluble vitamin—the latter is the more important. In my experience the neurotoxic element is ineffective in the presence of the protective factor. On the other hand, even in the absence of cereal, I have produced similar results in young dogs by feeding them on synthetic diets of pure protein, fat and carbohydrate, such as are given in rat experiments, when the vitamin A and carotene have been deficient. Zimmermann [3] has produced similar results in rats by giving them cereal-free vitamin-A-deficient diets.

(*b*) When cereal is replaced by potatoes, even when the diet is deficient in vitamin A, it is much more difficult to produce nerve lesions, and often the animals remain normal.

(*c*) The reason why yellow maize does not produce nerve degeneration is because it contains carotene as its pigment. White maize, not containing carotene, allows these changes to develop.

(*d*) Although the nerve degeneration changes described are not prevented by adding calcium salts to the diet, it seems probable that a great deficiency of calcium in the diet makes such changes worse. A diet containing only a small quantity of milk, or separated milk, and rich in cereals brings about abundant nerve degeneration, and since additional calcium in the form of calcium carbonate reduces this in amount, it is probably the result of a calcium deficiency. These animals develop very soft bones containing but little calcium salts, and quickly become paralysed. It is probably this condition which accounts for Stockman's recent results, in which he obtained demyelination changes in the cord of animals receiving diets rich in maize and other cereals, and deficient in calcium-containing foods.

Distribution of central nervous lesions.—In the absence of vitamin A and carotene, the nerve degenerative changes are especially seen in the spino-cerebellar tracts, the posterior tracts, and the anterior lateral columns. It is probable that the fibres principally affected are ascending, and that the crossed pyramidal tract usually escapes. The distribution of the degenerating fibres varies at different levels of the cord [2].

Above the medulla, spino-cerebellar fibres entering the cerebellum *via* both the inferior and the superior peduncles show degenerative changes. Other tracts affected include the fillet and the posterior longitudinal bundle.

Above the mid-brain the number of fibres showing myelin degeneration is greatly reduced, but it is quite clear from the behaviour of the animals that the higher parts of the brain do not escape the harmful effect of these diets. These animals when affected are stupid and incapable of fixing their attention on any definite object. In some cases, at least, the cerebral nerve-cells suffer degenerative changes, but this part of the nervous system has not yet been properly examined. Other nerve-cells, such as Clarke's column cells, Purkinje's cells, cells of the dentate nucleus, and, to a less extent, the anterior horn cells, are all apt to show chromatolysis, shrinking, excentric nuclei, and many glial cells in the immediate vicinity.

Changes in the peripheral nerves.—A more recent development of this experimental work is the discovery that the peripheral nerves are also involved in similar degenerative changes [4]. It would indeed appear that most afferent nerves suffer myelin degeneration. Thus the vestibular and cochlear divisions of the eighth, the optic nerve, the ophthalmic division of the fifth and the sciatic nerves when stained by the Marchi or Scharlach method show characteristic degeneration. At least in the early stages, and before paralysis develops, the efferent nerves seem to escape. This fact becomes evident on examination of the anterior and posterior roots of the cord. As a general rule, the anterior roots of animals brought up on these vitamin A-deficient diets are free from degenerating fibres while the corresponding posterior roots are greatly affected.

These changes in the afferent nerves are probably of great significance, especially in relation to the increased susceptibility of epithelial surfaces to infection which develops when diets are deficient in vitamin A [4].

Have the foregoing facts any relation to subacute combined degeneration of the cord?—Here again, as has happened on several occasions in recent years, we see a series of morbid lesions produced experimentally in animals by certain defined conditions showing a close similarity to a well-recognized disease found in man, and it is our duty to see whether the ætiology of the animal and human diseases respectively bear any relation to one another.

It can be said at once that, if there is any such relationship between the animal experiments just described and subacute combined degeneration of the cord in man, it cannot be as direct, as appears to be the case between these experimental results

and such nutritional diseases as convulsive ergotism, pellagra and lathyrism. In all the latter there is strong evidence that a vitamin-A deficiency, associated with excessive intake of some foods containing neurotoxic elements, accounts in large part for the nerve lesions. This suggestion does not, of course, preclude the possibility of other factors being also involved. In subacute combined degeneration, however, the complete absence of vitamin A from the food or from the body is unlikely, and since the experimental lesions only develop in animals when there is little or no vitamin A stored in the body, this single explanation cannot alone account for the clinical condition.

Because a substance such as vitamin A is present in the food, it does not mean that it is effective. It may not be stored in the body, or it may not be transferable to some seat of action, or its effectiveness may depend on the presence of a correct amount of some other chemical agent. It can be stated definitely, however, that not only does subacute combined degeneration develop when there is vitamin A in the diet, but also that this substance is stored in the liver in this disease, so that, if it is ineffective, it is for some other reason.

It is, however, only with much hesitation that I advance an argument of this type, because we have in recent times become so accustomed to see the specific effects of deficiency and excess of certain substances of physiological importance that it is difficult to imagine conditions where they are ineffective when present or, when absent or deficient, that processes which they control can be normal. Such occasions do arise, however, as, for instance, in diabetes mellitus, when the pancreas contains insulin which is relatively ineffective. We know also from the work of Houssay that whether insulin is active or not depends on the condition of the pituitary body, and the loss of the pituitary gland greatly increases the susceptibility of the animal to insulin. Thus removal of the pancreas does not produce diabetes in an animal deprived of its pituitary body.

Another instance of a similar nature is seen in the case of thyroxine, a substance which in minute quantities raises the basal metabolic rate of normal animals. In patients with nephrosis, however, it is difficult to raise their metabolism by this means. Thus there are analogous cases which show that the effectiveness of specific active principles can be modified by other metabolic changes.

Now it happens that in subacute combined degeneration, whatever the metabolic basis at fault, there is good evidence which shows that chemical elements quite sufficient in amount in the normal body to carry out their function, are insufficient to work effectively in controlling the nervous tissues. Thus it is generally accepted that the amount of liver or liver extract sufficient to improve the blood condition in pernicious anæmia to one approaching normality, say with a hæmoglobin reading of 80%, is insufficient to prevent the onset of subacute combined degeneration or to improve it, if it has already developed. Some claim, however, that, if the hæmoglobin content of these patients be increased to 100% by giving huge amounts of liver extract, the nerve disorder is prevented, or improved if present. Thus, even if we accept the view that the chemical agent responsible for the blood improvement and the nervous system control is the same, it is obvious that in these associated diseases very much larger quantities of this substance are necessary for the protection of the nerve metabolism than for improvement of the blood condition—a quantity out of all proportion larger than that effective in the normal man.

Or take the iron treatment as recommended by Sargant [6]. The body is loaded with iron in pernicious anæmia at a time when the blood condition is bad and subacute combined degeneration is developing rapidly. If Sargant's deduction from his results is correct—that excessive iron therapy in the form of 120 to 150 grains of Blaud's pill daily—greatly and specifically improves the nerve disorder, this can only mean that the stores of iron already present are ineffective. Whether we assume, therefore, that excessive liver principle or excessive iron acts in a

preventive or curative way in subacute combined degeneration, it is clear that ordinary or normal quantities of these substances are ineffective in preventing or curing the nerve condition. Now the present experimental work indicates that the cord-changes are not controlled by the water-soluble fraction of liver which cures the blood condition, but that they are controlled by a fat-soluble fraction of liver, namely, vitamin A. I have found in animal experiments that water-soluble fractions of liver which are curative of the blood condition in pernicious anæmia do not prevent central and peripheral degeneration of medullated nerve-fibres. The fat-soluble fraction of liver, on the other hand, has this effect. Incidentally it may be added that desiccated pig's stomach also does not prevent demyelination of nerve-fibres in these experimental animals.

Thus, both from the positive and the negative side, the experimental evidence on animals supports the view that myelin degeneration of medullated nerves in subacute combined degeneration is dependent on the ineffective action of a fat-soluble fraction of the liver and not on the water-soluble factor of liver or on the enzyme of desiccated stomach. Thus, on the analogy of the excessive liver extract and iron therapy combined with the animal experimental results, it may well be that vitamin A, although present in the liver of these patients, cannot, for some unknown reason, carry out its ordinary work of controlling nerve function and structure.

It will be asked, however, whether there is any clinical evidence that vitamin A or carotene given in excessive amounts, as in the case of liver extracts or iron, effects beneficially subacute combined degeneration, or even whether their influence is of any significance in this disease. There is certainly no good evidence of this at present. Cases of subacute combined degeneration under my care have never been given a diet whose only good quality was its high vitamin A content. I have always given them whole liver in large quantities together with other dietetic substances of high biological value, and although my experience is small, my impression is that such diets have proved effective both in staving off the nerve derangement and improving the condition of those who have developed the disorder. The diet I give, besides containing ½ lb. mammalian liver daily, includes 2 pints of milk, one or two eggs or their yolk, abundant vegetables, especially green vegetables, and cod-liver oil, ½ ounce. It is obvious that the beneficial effect on subacute combined degeneration of such a diet cannot be ascribed solely to its vitamin A and carotene content. Although I cannot give any direct clinical evidence of the suggestion, based on the animal experiments, that vitamin A is an ætiological factor of importance in this disease, I have never felt justified in the treatment of these patients to disregard the experimental evidence and its possible significance. Nor do I consider that it is right, on the basis of our present knowledge, to give such patients liver extracts without taking into account the rest of the diet. Indeed, it seems to me probable that the amount and severity of subacute combined degeneration that is described as occurring nowadays may be due to the giving of liver extracts only, which improve the blood condition and lengthen the life of these patients without preventing the nerve degeneration.

Before leaving this aspect of the subject, it may be well to mention that in the case of the only two post-mortem examinations of pernicious anæmia with subacute combined degeneration of the cord that I have personally seen during the last few years, the cause of death was pyelonephritis. The possible significance of this lies in the fact that pyelonephritis is a common occurrence in vitamin-A-deficient animals. The livers of both of these patients contained vitamin A, so that if vitamin A is of any importance in the condition under discussion, it must be concluded that it was ineffective both as regards the condition of the kidneys and the nervous system, either because it could not be mobilized or because it could not be used by the respective cells.

In conclusion, let me say a few words as to what would be expected to result from dietetic treatment in subacute combined degeneration, especially in established

cases. Dr. Carmichael has emphasized in his recent work that the peripheral nervous system is largely involved in this disease and that in curative results that are seen nowadays it is primarily changes in the peripheral nervous system that account for the improvement. Similar results have been described by Baker, Bordley and Longcope [5] in a series of cases of subacute combined degeneration.

In my experimental animals also, as mentioned above, the afferent peripheral nerves as well as those of the central nervous system show degenerative changes. Whereas certain early changes in the peripheral nerves, such as those found in the ophthalmic division of the trigeminal nerve associated with early xerophthalmia, heal up quickly on giving vitamin A, more severe degenerative changes may take months before the demyelination clears up and the nerve function is completely restored. I mention this fact because, as pointed out by Baker, Bordley and Longcope, many clinicians seem to expect curative results too quickly from the treatment of subacute combined degeneration of the cord. Where fibres in whole areas of the cord have disappeared, it would not be expected that any form of therapy would restore this function. On the other hand, it would be definitely expected that peripheral nerve lesions would clear up. Even in this case, however, if these are severe, such improvement would not be expected until after months of treatment. Baker, Bordley and Longcope say that nine months may be necessary. If continuous dietetic treatment cures, as it is now known to cure, the peripheral nerve lesion, it is probably safe to assume that the cord degenerative changes are stopped. Thus, even in severe cases of subacute combined degeneration, beneficial effects may be expected from this type of treatment, due both to the recovery of peripheral nerves and to the prevention of further central degenerative changes.

To sum up the present position in the light of the experimental and clinical work referred to above, it would appear that—

(1) The nervous system is greally influenced by nutritional factors, since it is possible to produce in young animals demyelination changes in medullated nerve-fibres of both the central and peripheral systems, which are similar to—probably in many respects identical with—those of convulsive ergotism, pellagra, lathyrism and subacute combined degeneration, i.e. the well-known toxic degenerations of the nervous system. In these experiments absence of vitamin A and carotene from the diet is the chief factor, but the condition may be hastened by adding cereals or cereal products such as embryo or ergot.

(2) Whereas these results probably account largely for the nerve lesions in convulsive ergotism, pellagra, and lathyrism, they cannot alone explain the nerve lesions of subacute combined degeneration, because in this disease the body contains vitamin A.

(3) If the animal experiments mean anything in relation to subacute combined degeneration—and the close similarity of the peculiar lesions suggest that they must do so—it can only be assumed that, for some unknown reason, vitamin A cannot be mobilized or cannot carry out its normal function in ordinary quantities in this disease. Reasons have been given to show that some other essential chemical substances in the body are also relatively ineffective in this disease.

There is clearly a gap to be bridged between the experimental and clinical knowledge. What is wanted is knowledge as to those conditions which prevent vitamin A from acting in the body in ordinary quantities. I know of no such conditions as yet. Possibly the associated condition, in subacute combined degeneration of achylia gastrica, may afford the clue to the missing link. However, I have never yet seen this condition in my experimental animals.

In the meantime it seems to me that experimental work of this type may ultimately lead to the solution of the clinical problem, and that the results ought to be regarded at least as of possible significance. Such patients should therefore be given not only the water-soluble fraction of liver known to cure the blood condition,

but also large quantities of vitamin A, either in the form of substantial quantities of whole liver or its fat-soluble fraction, such as mammalian or fish oil, as well as milk, eggs and green vegetables.

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Dr. E. A. Carmichael: Recently at the National Hospital, by the kindness of my colleagues and of Professor Fraser, and with the co-operation of Drs. Elliot and Golden, a study has been made of this disease, its symptomatology, its pathology, and the value of different forms of treatment.[1] In all, forty-three cases with involvement of the nervous system have been examined and treated during the last three years. Owing to the difficulty in diagnosis, the criteria have been made very rigid. Symptoms and signs referable to the nervous system have had to be symmetrical in distribution, and in all cases an alteration of reflex activity or an objective disturbance of sensation has been demanded. Cases with paræsthesia alone have not been included. The study has also been limited to those cases in which symptoms have commenced after the age of forty; the post-mortem records of the hospital contain the records of only two out of thirty-four cases in which the symptoms were present before the age of forty. Particular attention was paid to the blood picture, for there is no satisfactory evidence in the literature that subacute combined degeneration occurs in association with any other anæmia than that recognized as macrocytic. Accordingly in all cases the presence of a macrocytic anæmia has been established by means of a blood-count and a Price-Jones curve. An absence of free hydrochloric acid in the stomach-contents following an alcoholic test meal and a subcutaneous injection of histamine was a necessary finding. The findings on examination of the cerebrospinal fluid and the Wassermann reaction of the blood were normal. To these investigations was added the necessity of demonstrating a reticulocyte response in the blood following the administration of a substance known to be rich in hæmopoietic factor. In cases where any measure of therapy was being tested, blood-counts, including reticulocyte counts, were made every day or on alternate days; and precautions were taken to exclude from the diet food known to contain a hæmopoietic factor, and also red meat. Examination of the nervous system was made at frequent invervals by one of two observers alternately, and wherever possible quantitative measurements were made.

In this series most improvement has occurred in the marked amelioration of the subjective sensory disturbances to the point of complete cessation. It has not been our good fortune to see any case of dramatic improvement, and in no case has an extensor plantar response become flexor; there has, however, been a return of tendon reflex activity in six cases. Muscular power and co-ordination also improved in many; these latter improvements were coincident with the betterment of the blood picture and of the general well-being of the patient, and it has been impossible to obtain unequivocal evidence that they resulted from a change in the nervous lesions.

With regard to the site and nature of the lesions in the nervous system: In the spinal cord, the lesions are situated chiefly in the postero-lateral columns and are characterized by a defect in the myelin. The myelin sheath becomes distended and eventually disappears; this process, as seen microscopically in early and late lesions, is entirely different from that present in cases of disseminate sclerosis and similar demyelinating diseases. Along with the myelin destruction, but to a lesser degree, considerable destruction of axis-cylinders takes place. Difficulty is thereby encountered in expecting any substantial improvement with regard to the symptoms

[1] Undertaken on behalf of the Medical Research Council.

and signs referable to the spinal lesions; admittedly it may be possible for some slight degree of recovery to take place, especially in early lesions.

In this series, the majority of patients complained of a numbness, tingling, or "pins-and-needles" sensation referable to the periphery of the two lower or two upper or all four limbs. These subjective sensations were more intense at the periphery, grading off proximally. In the absence of such spontaneous paræsthesia, they could be frequently invoked by light pressure on the fingers and toes. Vibration sense measured quantitatively showed a greater departure from normal at the periphery of the legs, with little or no involvement over the sacrum and at the anterior iliac spines. Tenderness of the calf muscles was no uncommon observation as tested with an algometer. Reflex activity in the majority of cases was lost at the ankles or at both ankles and knees. Following adequate treatment, sufficient to bring the red-cell count to 5,000,000, the subjective and objective cutaneous sensory disturbances diminished. When these were of recent origin the rapidity of recovery was marked; on the other hand, when they were of long standing, several months frequently elapsed before substantial improvement took place. In each of the six cases in which alteration of reflex changes was observed, it was in the nature of the return of the knee-jerks or the ankle-jerks previously absent. An improvement has been observed in the vibration-sense when the loss was limited chiefly to the periphery and the threshold for the production of pain in the calves has become raised.

In attempting to explain such observations certain difficulties were encountered when the pathological process was accepted as being situated only in the spinal cord, and the suggestion that a lesion in the peripheral nerves may be present appeared worthy of further investigation. McAlpine [1], in reviewing his results, suggested that the peripheral nerves may be involved and recently Baker, Bordley and Longcope [2], have drawn attention to the fact that some of the symptoms and signs are possibly dependent upon changes in the peripheral nerves. Reports of the microscopical examination of peripheral nerves in this disease are scanty. In their original article, Russell, Batten, and Collier [3], described changes in one case in the large mixed nerves of the leg. Matthieu [4] observed in one case marked "beading" of the myelin sheaths of the sciatic nerve. Hamilton and Nixon [5] found degeneration of the peripheral nerves in six cases by the Marchi method of staining. This work is open to the criticism that Marchi methods for staining the peripheral nerves are unreliable owing to the ease with which artefacts may be produced by incautious handling. Again, as the material was from the post-mortem room, the slight changes noted might be of recent origin, the result of a terminal infection or cachectic state. The same criticisms may be levelled at the observations of Dana [6], Nonne [7], and Lloyd [8], who found changes in the posterior roots. During this study the microscopical examination of the terminal branches of the anterior tibial nerve was carried out in several cases before any treatment had been given. As yet the examination of these nerves is incomplete. In one case with very marked subjective peripheral sensory disturbance, changes have been found in these small nerves. There was a marked absence of myelin and the myelin present was unhealthy. Following the intramuscular administration of liver extract in this case, marked improvement occurred in the peripheral subjective sensations. In another case, there appeared a similar condition but to a less degree. Though the work is in its early stages, the evidence is suggestive—almost confirmatory—of the involvement of the peripheral nervous system in this disease.

As to therapy, the experimental work of Mellanby [9] raises the question as to whether some of the lesions in the nervous system in cases of subacute combined degeneration may or may not be in the nature of a degeneration following an avitaminosis. To this must be added the knowledge that in pellagra changes similar to those found in cases of subacute combined degeneration of the cord are found at

post-mortem examinations. Several cases of this series have accordingly been treated with large doses of vitamin A after maximal improvement with liver had been obtained, but no further improvement has been manifest. It is possible, however, that the liver contained a sufficient quantity of vitamin A. Three cases have been given daily 120 grm. of marmite for fourteen days and then marmite extract for another fourteen days. As no improvement resulted in the nervous signs or symptoms and only a minimal but temporary improvement in the blood condition occurred, it was considered undesirable to persist with this form of therapy. The addition of marmite to the diet in several cases in which the blood picture was raised to normality by liver alone has not produced any further beneficial effects upon the symptoms and signs referable to the nervous system.

Iron, in the form of Blaud's pill or ferri carbonatus saccharatus in daily doses of 120 gr. and over, has been given to three cases for a period of four or five weeks, at the termination of which there was no improvement in either the blood picture or nervous symptoms and signs; it was considered unjustifiable to persist with this form of therapy in these cases and liver was given with subsequent marked improvement in the blood picture and nervous subjective sensations. In two other cases similar doses of iron were given, following the administration of, and along with, one pound of liver for periods up to five months; at the end of this time neurological examination revealed no change for the better.

Throughout this work one observation stands pre-eminent, namely, the necessity for obtaining a blood-count of 5,000,000 in order to obtain full beneficial results. Frequent difficulty, however, has been encountered in obtaining such a blood-count with doses of liver sufficient to produce a marked reticulocyte response, and it has been necessary to increase the liver dosage or to supplement the liver diet with injection of potent liver extract. This failure to obtain a normal blood-count with ordinary doses is of importance, as instanced by one case in which there was a slow and steadily progressive involvement of the nervous system with a red-cell count of 4,300,000; when this count was raised to 5,000,000 a slight improvement set in. The cause of this failure to obtain the necessary blood-level may be due, according to Bebe and Lewis [10], to the presence of either high blood-pressure or an infection; in several cases of this series, showing this resistance to normal doses of liver, a low-grade infection of the urinary tract was found.

As to the relative value of liver extract given by mouth or intramuscularly, the number of cases treated by the latter method does not warrant a definite conclusion. Three cases treated by intramuscular injection of potent liver extract—and it is necessary to be sure of its potency—have exhibited extremely rapid improvement of the blood picture and of the subjective nervous manifestations, it is possible that the intramuscular injection of liver extract may be the most beneficial form of therapy.

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Professor F. S. Langmead: Owing to the fact that Dr. Sargant is unable to be present, I am allowed to speak in his stead, in order to introduce into the discussion the question of the treatment by iron of the nervous disorders associated with anæmia. Had this contribution been in his hands, he would have spoken with more precision and in greater detail of particular cases, and offered a more complete presentation of the subject. My claim to intervene is that many of these cases have been under my care and others under my observation.

Before relating our experiences I would make a plea for the consideration of neurologists. Would it not be more fruitful to consider as a whole the nervous phenomena which accompany anæmias than to limit ourselves to combined degeneration of the posterior and lateral columns in the strictly anatomical sense? If we consider only cases in which degeneration of the conducting fibres has actually occurred, the value of treatment is brought within narrow limits, except in the minds of those who believe in the possibility of regeneration, an attitude which, I think, few would adopt. Yet, unless I misread the textbooks and misconstrue the relatively limited cases in my own experience, there are stages in the disease which precede the degeneration strictly called combined degeneration of the cord, stages which can be ascribed to disturbed function of the peripheral nerves, and perhaps of the conducting fibres in the cord. The progress of many cases, I do not say of all, is from paræsthesias and minor losses of sensation, through grosser loss of sensation, loss of vibration sense and ataxia to the picture of the fully developed disease.

It surely is in the earlier phases that treatment is most likely to meet with success. If we wait until degeneration in the posterior and lateral columns is incontestable in the strictly scientific sense, we obviously wait, as far as our knowledge goes at present, too long. It would be better to jettison the term "subacute combined degeneration" than to visualize it in its strictly anatomical sense, if thereby progress is hindered, and the usefulness of active treatment discountenanced.

What we believe we have attained by the use of large doses of iron—by which I mean something in the neighbourhood of 150 to 200 gr. of Blaud's pill daily—is a very considerable and comparatively rapid improvement in the neurological symptoms and signs, which accompany the anæmias. In some cases the picture of the disease has not progressed sufficiently to provide undoubted evidence of degeneration, in others we believe that to be the right diagnosis. We do not claim that regeneration of the cord has been produced, nor that a plantar extensor response has been made flexor, but we hope that degeneration has been prevented. It can be no more than a hope at present, since the question is beyond the power of proof.

Within these limitations patients, whether suffering from subacute combined degeneration or from nervous phenomena short of that diagnosis, have been materially benefited. Some so incapacitated by their ataxia as to be confined to bed have been enabled to walk with little disability, and have returned to active life. Reflexes have reappeared. Areas of loss of sensation, including vibration sense, have disappeared. Indecipherable writing has again become ordinary. Fine needlework which had been abandoned has been resumed. But it must be emphasized that no claim to *cure* combined degeneration has been made. When these improvements have occurred in cases of subacute combined degeneration the diagnosis has not rested upon the opinion of Sargant and myself alone: the cases have been seen by Dr. Wilfred Harris and Dr. Denis Brinton, and a few by other neurologists, who have agreed with the diagnosis. The preparation must be fresh, finely ground up, put into capsules for easy absorption, and given over a period of from one to two months, before its value can be assessed.

The rationale subtending the treatment is merely hypothetical at the present juncture. The facts that the nervous phenomena may occur before the characteristic blood changes, that they bear no comparable relationship to the severity of the blood picture, and that re-establishment of a normal blood picture often leaves them unaffected, all point to a different process in their development from one which can be corrected by liver alone. Such an inference seems to me to be justified. The hypothesis which Sargant has mooted, that they are associated with faulty iron metabolism, and in some way dependent upon achlorhydria, may be the correct one.

On this hypothesis Sargant predicted, some months ago, that the nervous phenomena seen in pellagra might benefit by large doses of iron, and this forecast has received encouraging fulfilment by the cases reported by Professor A. G. Biggam and Dr. Paul Ghalioungui in the *Lancet*[1] recently.

It may be suggested that the results have been attained by psychical causes alone. In my opinion the personalities have been too varied and the results too constant with iron, and too slight with other treatment, for that to be an adequate explanation.

Whether the benefit will prove to be temporary remains for the future. The improvement, however, has been maintained for two years. In any case the results have been worth obtaining. An advantage of the treatment is the ease and economy with which it can be employed, which is in marked contrast to some other methods.

Dr. C. C. Ungley[2]: Before the discovery of liver therapy by Minot and Murphy [1] in 1926, subacute combined degeneration of the cord, although subject to occasional remissions, appears to have been an almost invariably progressive condition, fatal as a rule within two and a half years.

The following methods of treatment have been used: whole liver, liver extracts by mouth, desiccated stomach, brain, vitamin concentrates, iron, and liver extract by injection.

(1) *Whole liver*: In 1929 I reviewed with Suzman [2] 61 cases of subacute combined degeneration. Of the 30 patients treated with liver, 17 were improved, eight were unimproved and five died. The results in many cases were striking, in that patients with severe ataxia and paraplegia recovered sufficiently to be able to walk unaided and even to perform heavy labouring tasks.

When the total liver taken by each of the patients is calculated and the total length of treatment is known, it is possible to obtain an approximate estimate of the average amount ingested in a week.

It is significant that of 17 improved cases, 13 (76·5%) had taken up to 3½ lb., but never less than 1 lb. per week, and four had taken ½ to 1 lb. Whereas of the 13 patients who were unimproved or died, eight had taken less than ½ lb. per week, two had taken from ½ to 1 lb., and only three had taken an average of over 1 lb. per week.

With regard to maintenance doses, a recent follow-up of this series has further indicated that the disease can usually be held in check by whole liver therapy if the average amount ingested for long periods is well in excess of 1 lb. per week. In some cases much larger maintenance doses are required.

Of the 17 improved cases, 16 have been traced and of these:—

Eight patients have maintained their improvement and are able to walk as well as or better than they could when reported upon in 1928-1929. Two patients relapsed after reduction of dosage, but have recovered and are working again after treatment with parenteral liver extract. Six patients have died. In three instances the liver intake had been markedly reduced or actually discontinued. One patient is said to have died from severe anæmia without relapse of the neurological condition, after taking large amounts of whole liver and liver extract. In the two remaining cases no details of the liver intake or of the cause of death are available.

(2) *Oral liver extracts.*—Although good results have been obtained with whole liver, the reverse has been the case with commercial liver extracts, possibly due to insufficient dosage. In only one instance have I personally observed any benefit from oral liver extract alone in subacute combined degeneration, and this was with

1 *Lancet*, 1933 (ii), 1198.

2 From the Royal Victoria Infirmary, Newcastle-upon-Tyne; working with the assistance of a part-time grant from the Medical Research Council.

an extract which is prepared not by the usual method originated by Cohn [3], but from the pressed juice of liver.

(3) *Stomach preparations.*—My experience with this method is limited, but a survey of the literature indicates that desiccated stomach in adequate doses may be effective for the prevention and treatment of subacute combined degeneration of the cord.

(4) *Iron.*—In the only case in which I have given this method a fair trial, the administration of Blaud's pill in doses of 120 to 150 gr. over a period of ten months was followed by slight diminution of paræsthesiæ, and slight improvement in gait, but the patient remains ataxic and the neurological findings have undergone no significant alteration.

(5) *Vitamin concentrates.*—The administration of large doses of vitamins A and D (in the form of nine adexolin capsules daily) was without effect in the few cases of subacute combined degeneration in which it has been tried.

Marmite, yeast granules, wheat germ, and other sources of the vitamin-B complex have usually failed to produce neurological improvement even when administered in very large doses. In some cases the neurological condition became worse during treatment.

(6) *Brain.*—The results obtained with a diet of brain, which is only one-third as potent as whole liver for blood regeneration in pernicious anæmia, and the reasons for its use have been discussed [4]. With two exceptions, cases of subacute combined degeneration were selected which had proved refractory to whole liver administered in large doses, but in spite of this six of them improved with brain.

The findings supported the hypothesis that the effect of organtherapy upon the nervous system in this disease is not wholly dependent upon anti-anæmic potency, and it was pointed out that brain was unsuitable for the routine treatment of subacute combined degeneration, because of its low potency for blood regeneration.

(7) *Parenteral liver therapy.*—It would appear that certain liver extracts effective for blood regeneration may have little influence on the neurological manifestations of pernicious anæmia, except perhaps in enormous doses, and that a patient whose blood is being kept at or near a normal level with such an extract may develop subacute combined degeneration of the cord. Reasons have been put forward [4] for the belief that there may exist in liver and in brain a factor beneficial to the nervous lesions in pernicious anæmia, distinct from that which influences the regeneration of blood. If this is true, it does not follow that a given method will extract both factors equally well, and it seems desirable to recognize the existence of two chief types of commercial liver preparation :—

(*a*) Extracts prepared in the usual way by modifications of the Cohn process [3], in which the first step is the coagulation of proteins, and (*b*) those in which the initial process is to express the juice from liver by great pressure (several tons per square inch).

I have not, personally, been able to observe any significant neurological effect from liver extracts of the Cohn type, whereas excellent results have been obtained with Gänsslen's extract [5], prepared from the pressed juice. Other observers, however, have noted neurological improvement with parenterally administered extracts of the Cohn type which in this series have not yet been used in a number of cases sufficient for just comparison. Further work will be necessary to determine whether or not there is any significant difference in neurological effect when extracts of the two types are administered in doses hæmopoietically equivalent.

Gänsslen's liver extract is prepared from the juice obtained by subjecting liver to a pressure of several tons per square inch. Injected intragluteally, 2 c.c., derived from only 5 grm. of liver, are said to be as effective for blood regeneration as 500 grm. of whole liver by mouth.

Up to the present time nine cases of subacute combined degeneration of the cord have been under treatment with Gänsslen's liver extract (campolon) for periods of more than six weeks. All were undoubted cases of pernicious anæmia with evidence of marked involvement of the nervous system. Seven were males and two females, and their ages varied from 28 to 64 years.

	Under 40	40 to 49	50 to 59	60 and over
Cases:	2	2	4	1

All patients showed the characteristic megalocytic hyperchromic blood picture, and a histamine-refractory achlorhydria, with little or no pepsin.

The duration of neurological symptoms before treatment with Gänsslen's extract varied from one month to seven years.

	Under 6 months	6 to 11 months	1 to 2 years	2 to 4 years	Over 4 years
Cases:	2	2	3	0	2

In some cases oral liver therapy had been given previously. (One patient had taken 2 to 3½ lb. (960 to 1,680 grm.) of liver a week for nine months with slow improvement. In two cases the liver therapy had at first been adequate but the neurological condition had relapsed after reduction of dosage. In three instances the liver had been taken only in grossly inadequate amounts—i.e. less than 1 lb. (480 grm.) a week, together with small amounts of liver extract. Of the remaining patients, two had not had liver therapy, and the other none for sixteen months.)

Gänsslen's liver extract (campolon) has been given intragluteally for periods of from six to twenty-five weeks, usually in doses of 6 or 8 c.c. on alternate days. The average amount per week for the whole period of treatment was from 14 c.c. to 27·1 c.c.

AVERAGE AMOUNT PER WEEK.

	Under 15 c.c.	15 to 20 c.c.	20 to 25 c.c.	25 to 30 c.c.
Cases:	1	3	3	2

In eight instances the injections are still being given.

The total amount varied from 98 to 444 c.c., derived from only 245 to 1,110 grm. of fresh liver.

Three patients received whole liver for from five to nine days at the commencement of campolon treatment and two for a few days after returning home while continuation of parenteral therapy was being arranged. With these exceptions no liver, stomach, iron or other known potent material was administered. With one exception (Case 1) no massage or re-educational exercises were given, but patients were encouraged to attempt to walk for a short period daily.

The usual improvement in symptoms referable to anæmia and to disorders of the alimentary tract which occurs during remissions, however induced, was noted in all cases. A reticulocyte crisis was observed in cases with initial erythrocyte counts below 3·0 millions. The red blood-cells and hæmoglobin values are summarized below.

RED BLOOD-CELLS.

	Under 2·0	2·0 to 2·9	3·0 to 3·9	4·0 to 4·9	5·0 to 5·9	6·0 and over
Before treatment	3	3	3			
After treatment			1	3	2	3

HÆMOGLOBIN (SAHLI LEITZ: 100% = 13·8 GRM. PER 100 C.C.).

	Under 40%	40 to 49	50 to 59	60 to 69	70 to 79	80 to 89	90 to 99	100 and over
Before treatment	2	2	1		1		3	
After treatment				1		1	4	3

Results.—Neurological improvement has occurred in all of the nine cases. The table shows the symptoms and signs which were present and the effect of treatment. It is interesting to compare these results with those of Baker, Bordley and Longcope

[6] who found that oral liver therapy given for more than ten months in eight cases of outspoken subacute combined degeneration of the cord was followed by improvement in 58·93% of the signs and symptoms of involvement of the nervous system.

SIGNS AND SYMPTOMS OF NINE CASES OF SUBACUTE COMBINED DEGENERATION BEFORE AND AFTER TREATMENT WITH GÄNSSLEN'S LIVER EXTRACT FOR FROM SIX TO TWENTY-FIVE WEEKS.

	Cases	Well	Improved	Unimproved
Numbness and tingling	9	3	6	—
Romberg's sign	5	4	1	—
Incoördination :—				
Upper limbs	2	2	—	—
Lower limbs	9	4	3	2
Impaired joint sense :—				
Fingers	3	3	—	—
Ankles	5	1	1	3
Toes	9	—	6	3
Absent vibration sense	8	—	4	4
Impaired vibration sense	1	—	—	1
Impaired cutaneous sense	7	3	4	—
Absent or diminished knee-jerks	5	3	1	1
Absent ankle-jerks	5	—	—	5
Increased deep reflexes	3	1	—	2
Plantar extension :—				
Definite	5	—	4	1
Doubtful	1	1	—	—
Dysfunction of hands	3	2	1	—
Sphincter disturbances	7	5	1	1
Psychic disturbances	2	2	—	—
Total observations	89	34	32	23

Signs and symptoms improved: 74·16%.
Signs and symptoms unimproved: 25·84%.

The effect of treatment upon individual signs and symptoms will now be considered in more detail.

Mental disturbances.—Disorientation disappeared in one case, possibly due to relief of the anæmia. In another patient a severe anxiety neurosis has given place to a cheerful and apparently normal mental disposition. Both of these patients and also one other suffered from impairment of memory, which has cleared up in each case.

Paræsthesiæ.—Numbness and tingling in the extremities, present in every case, have disappeared entirely in three cases, diminished in extent and intensity in four, while in the remaining two the intensity has diminished but not the extent. Quite commonly there has been an initial increase in the severity of the numbness and tingling during the early stages of treatment.

Romberg's sign, which was strongly positive in the five patients who were able to stand alone, has become negative in four instances and less marked in one. In four cases it was impossible to apply Romberg's test because the patients were unable to stand without assistance. One is not yet able to do so, and in the remaining three the sign is markedly positive.

Incoördination and loss of muscle sense in the lower extremities, present in all cases, and usually gross, has cleared up entirely in four cases and in three more has improved considerably. Coördination of the upper limbs, which was impaired in two instances, is now normal in each case.

Joint sense.—The sense of position of the joints of the fingers has returned to normal in the three cases in which it was impaired. Joint sense in the ankles, which was grossly impaired in five cases, is normal in one patient, much improved in another, and unimproved in three. Joint sense in the toes, absent or defective in all cases, has shown moderate or slight improvement in six and no change in three.

Vibration sense (as tested with a C. 256 fork) was absent in the lower limbs in eight cases and diminished in one. In cases in which the patient was not a good witness it was difficult to find the upper level of the loss, but six patients were unable to appreciate vibration in the pelvis, and in five of these the loss extended to the lumbar or lower dorsal vertebræ. In four instances there has been a return of vibratory sense in some or all of the areas where it was formerly absent, but in no case has this form of sensation become entirely normal.

Cutaneous sensibility to touch and pin-prick, which was impaired in the lower limbs in seven cases, has become normal in three and much improved in four.

The knee-jerks were absent in four patients, in three of whom these reflexes are now active, while in the fourth they are present but sluggish. In a fifth patient the knee-jerks were diminished but not absent, and remain unchanged.

The ankle-jerks have not returned in any of the five patients in whom they were absent.

Exaggerated knee- and ankle-jerks observed in three cases, have become normal in one and remain unchanged in two.

Plantar reflexes.—In four cases marked extensor responses (obtainable on stimulating either side of the sole of the foot) were present bilaterally. In three of these patients the degree of Babinski reaction is diminished, in that the reflex is more difficult to obtain and the area of sole from which dorsiflexion of the great toe can be elicited by stimulation is reduced to the outer border of the sole. In the fourth case a complete return to a flexor type of response has occurred on one side the reflex on the opposite foot being unaltered.

In one other case both plantar reflexes were doubtful, one being pathological and probably extensor. Both reflexes are now definitely flexor.

Observations upon the character of the plantar reflexes, as also of the other neurological findings, were repeated at short intervals. The changes noted above occurred gradually, and were checked by the observations of other physicians.

Three patients had gross *dysfunction of the hands*, with impairment of ability to write, knit, etc. In two of these patients coördination of the upper limbs was disturbed, while all three showed astereognosis (marked in one, slight in two), and diminished joint-sense in the fingers. In two instances the function of the hands has become normal, while the third patient is able to knit and to write, but has some astereognosis in one hand.

Sphincter disturbances, which occurred in seven cases, have disappeared in five and diminished in one. Incontinence of urine has ceased in four and precipitancy in two patients in whom these symptoms were present before treatment. In only one of these patients is there any remaining sphincter disturbance, consisting of some difficulty in passing urine. In the seventh case slowness of micturition remains unchanged.

Difficulty in walking has diminished in all cases. Of four patients who were unable to stand, one walks with help, and three although somewhat ataxic, can walk alone for distances of about 15, 50 and 200 yards respectively.

Of two patients who were able to walk only with help, one has a normal gait and the other is slightly ataxic on turning sharply. Both can walk easily for many miles. One patient who could walk only when leaning heavily on a stick, now has a normal gait, and in the course of his work as a canvasser walks 10 miles a day without difficulty.

Of two patients whose gait was ataxic but who could walk alone, one is less ataxic and the other walks normally. The latter patient works in the shipyards and can step with confidence along narrow planks at a considerable elevation.

Conclusions

Prophylaxis.—An important point in the treatment of pernicious anæmia is that the maintenance dose of potent material should be adequate to prevent the development of subacute combined degeneration. This may be attained by the use of whole liver, desiccated stomach or liver extracts, but with the latter in particular the amounts should be in excess of the minimum required to maintain a normal blood picture. Temporary cessation of treatment, or even reduction of dosage, is often dangerous and may be followed by the rapid development of funicular myelopathy.

Treatment.—On the basis of the results reported here and elsewhere [2] the following recommendations are put forward for the treatment of subacute combined degeneration :—

(1) Injections of Gänsslen's liver extract in doses amounting to 20 to 40 c.c. a week until the patient is able to walk well alone. During this period the patient should be encouraged to attempt to walk daily, even if the assistance of two persons is required. The dose is adjusted to the requirements of the individual case. If the neurological condition remains stationary after five or six weeks on a given dose, the amount should be doubled or trebled, even if the red blood-cell count and hæmoglobin value are normal or supranormal.

(2) Subsequently raw liver pulp ½ lb. (240 grm.) daily. In many cases the improvement may be maintained by doses as small as 1½ lb. (720 grm.) a week, but for safety the lowest maintenance dose allowable should be 2 to 2½ lb. (960 to 1,210 grm.) a week. Desiccated stomach or periodic injections of liver extract may be used instead of raw liver, but in any case the dose of potent material should be much in excess of the minimum required to keep the patient free from anæmia.

(3) Any return of neurological symptoms, even if merely an increase of numbness and tingling (and any fall in the red blood-cell or hæmoglobin level below 4·5 millions or 85% hæmoglobin) should be an indication for the resumption of massive dosage, either parenteral or oral, until the relapse has been checked.

(4) The occurrence of vomiting, nausea or other digestive symptoms liable to interfere with the ingestion or absorption of potent material is frequently followed by an exacerbation of the neurological condition, and should be met by parenteral therapy.

(5) As in diabetes, the elimination of septic foci is of the utmost importance. The supervention of any infective condition, e.g. "influenza," septic conditions of the urinary tract, etc., should indicate a large increase in dosage, either parenterally or orally.

(6) No case of subacute combined degeneration, however severe—even if associated with bed sores and incontinence with infection of the urinary tract—should be abandoned without resource to the administration of maximal doses of potent material over a long period.

From this brief preliminary communication acknowledgments, case reports, and a review of the literature have purposely been omitted.

[*The results were demonstrated by means of cinematograph pictures showing the condition of the patients before and after treatment.*]

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Dr. F. J. Nattrass said that with reference to the criteria mentioned by Dr. Carmichael, Dr. Ungley had closely followed those, with the exception of that concerning age, as he and his colleague had had some cases in which they were satisfied with the diagnosis of subacute combined degeneration, in people under 40 years of age. To his knowledge, Dr. Ungley's observations had been carefully carried out, and his results were very moderately stated.

In his (the speaker's) view, there could be no question that campolon, by intramuscular injection, had superseded the most effective form of treatment which had been hitherto utilized, namely, raw liver pulp.

With regard to alteration of physical signs, there was no doubt that extensor responses, in a certain number of cases, had become flexor; he had satisfied himself as to this on several occasions, notably in one severe case illustrated by Dr. Ungley on the screen. He had seen that patient in the first instance, and had followed her case through the entire course. With regard to knee-jerks, sometimes these, after being absent, had returned, and in other cases exaggerated knee-jerks had become normal. In a patient shown at this meeting the ankle-jerks had disappeared during the course of his improvement. Whatever the explanation, and however valuable the changes in the physical signs as evidence of some change taking place in the spinal cord, they were not so impressive to the clinical observer as the notable improvement in the muscular power and in the coördination. Such changes in these particular physical signs bore little relation to the clinical improvement of the patients. While in the majority of cases plantar responses, whether extensor or flexor, remained unchanged during the course of treatment, the patients regained power and coördination and finally walked more or less perfectly.

It was difficult for the clinician—for himself, certainly—to believe that the improvement in these cases could be attributed completely to the repair of the peripheral nerves. The picture was clinically unlike that of polyneuritis; cases with exaggerated knee-jerks and extensor plantar responses improved in the same way as those in whom the deep reflexes were lost; there was no suggestion of any lower motor neuron palsy or atrophy, and the distribution of the loss of joint sensibility and vibration sense was more extensive in the disease under discussion than in polyneuritis. Paræsthesia, in some cases, extended to the waist, and as the patient improved it descended until it reached the periphery, and then disappeared.

Lastly, he considered that the explanation of the difference in results which had been recorded in subacute combined degeneration was attributable to a difference in dosage. While good results had been recorded in many cases, especially in America and Germany, the reports in this country in general had not been very encouraging. Dr. Ungley gave much larger doses and for a longer period than was usual. That, with no other treatment except steady encouragement of voluntary effort, accounted for the high proportion of Dr. Ungley's successful results.

Dr. Fergus R. Ferguson said that the striking features which had been noticed previously—and which had been emphasized by the reports of the opening speakers—were the extraordinary differences in the results obtained with similar forms of treatment—liver, iron, etc.—by investigators in different parts of the country. In the case of iron therapy, apparently, exactly similar doses and preparations had been employed; so marked were the differences in results that one was tempted to suggest that somewhat different—though allied—conditions were being discussed.

He would like to draw attention to the value of stomach preparations—pepsac, extomak, etc.—which he, together with Dr. Wilkinson, was accustomed to use.

With regard to the part played by vitamin deficiency in the production of subacute combined degeneration of the cord, he had an interesting case under his care. The patient was a woman of 42, who at the age of 15 had begun to have epileptic attacks. She had various forms of medicinal treatment without much success until fifteen

years ago when she was advised to restrict her diet and told that it must not contain any meat, vegetables, butter, fresh fruit or sweets. The frequency of her epileptic attacks was reduced after she began this treatment, so that she adhered strictly to the diet. Eighteen months ago paræsthesiæ and pains in the limbs developed. Examination showed absent tendon-jerks in the legs, with extensor plantar responses and the clinical features of a well-established case of subacute combined degeneration of the cord. Under a diet containing large quantities of vitamin A, stomach extract and iron, she has made an excellent recovery and is now walking well.

Dr. Wilfred Harris said that Professor Mellanby had put forward a view such as one would expect from an experimentalist, but he was surprised that Dr. Carmichael did not criticize the statement that cord lesions could not heal. If a nerve-fibre of the cord was dead it was dead, and there was an end of the matter; but it was a different matter with cord symptoms. A case of acute myelitis might be paraplegic and completely anæsthetic to the nipple: was that a cord lesion, or was it a lesion of a peripheral nerve—seeing that the patient might recover so well that one could not tell any difference in gait? Did that not prove that the spinal cord lesion had been healed? The damage had not killed the nerve-fibre; it had only knocked it out in regard to its function. Cord symptoms could improve enormously. The same could be said of the cases of the kind under discussion which were being treated. The case he had hoped to show to-night was, as he was sure Dr. Carmichael would have agreed, one of subacute combined degeneration, except for the anæmia; why should that diagnosis be denied just because there was no megalocytic anæmia? What right had anyone to exclude a disease because one pathological condition was so far absent? He might as well say a case was not tabes because there was no optic atrophy. There was need to be more catholic in diagnosis. One could not carry out a post-mortem examination as a preliminary to making one's diagnosis, though possibly some people would like to do that!

With regard to treatment, accounts of extraordinary improvement had been given from various sources. He wished to put in a plea for the recognition of the value of iron in these cases; he had seen many cases which showed remarkable improvement under iron therapy. One patient was becoming worse under liver treatment, and had megalocytic anæmia, but she recovered under extraordinarily large doses of iron. One man had been growing worse for three years, and had paræsthesia. When he (the speaker) saw him he was paraplegic, and had sphincter weakness. After having large doses of iron he recovered and could walk fairly well, but his response was still extensor. Years of work would show that there was more than one drug which would do good in this condition.

He would have liked to hear more of the significance of the occurrence of achlorhydria in these cases; it seemed to be a very frequent if not an essential symptom.

Dr. Hugh Stannus said the subject interested him from the point of view of tropical medicine, more especially in relation with pellagra, in which a condition closely resembling subacute combined degeneration of the cord had been demonstrated by Dr. Kinnier Wilson.

He would be interested to hear from Professor Mellanby whether the degenerative lesions, occurring in the cords of his experimental animals fed on a deficient diet, persisted after the animals had later received an adequate diet containing the necessary vitamins?

It would be remembered that in the polyneuritis of pigeons the symptoms might disappear half an hour after the administration of vitamin B_1, but the lesions in the nerves, which gave the condition its name, persisted. These lesions were therefore not the cause of the symptoms.

He would also like to know whether Dr. Carmichael had examined the nerves from any case of subacute combined degeneration of the cord after treatment and restoration of function.

Dr. L. J. Witts said that his own experience confirmed the remarkable improvement which sometimes occurred in advanced forms of subacute combined degeneration, and the value of large doses of intramuscular liver extract.

No one in the discussion so far had spoken of prophylaxis, yet this was a question of the utmost importance. Although, as Dr. Nattrass had said, the general results in this country had not been encouraging, he would like to mention the results of Dr. J. F. Wilkinson, who had the largest experience of pernicious anæmia of any man in this country, and who had had 264 people under treatment for periods extending up to three and a half years, not one of whom had developed subacute combined degeneration. These patients were all treated with desiccated stomach by mouth. The only way in which subacute combined degeneration could be prevented was by keeping patients with pernicious anæmia under continuous observation and controlling treatment by the changes in the blood and the central nervous system. For that reason most of the published papers on pernicious anæmia and subacute combined degeneration, which were merely casual surveys of patients not seen for long intervals, were worthless, for everybody should know by now that subacute combined degeneration almost inevitably developed if pernicious anæmia was inadequately treated.

From the few really careful studies of the disease, it was apparent that subacute combined degeneration could always be prevented, could usually be arrested, and could often be materially improved, by proper treatment. In theory, the form of therapy or effective substance employed was perhaps unimportant, as long as the dosage was sufficient. In practice, whole liver had proved a failure, as it was impossible for most patients to eat enough of it. If people who lauded the virtues of whole liver would eat 1½ lb. of liver a day for a week, for that was the kind of quantity required by patients with subacute combined degeneration, they would be less enthusiastic in recommending whole liver in future, and would sympathize with the patient who quoted appropriately from the Book of Job, "That which my soul abhorred is now become my sorrowful meat." Liver extracts for oral use were expensive, and it was doubtful whether some of them contained the principles which were necessary for the health of the nervous system. Intramuscular extracts of the "campolon" type were ideal but had the practical disadvantage of injection. He would therefore like once again to emphasize the value of desiccated stomach in the prophylaxis and treatment of subacute combined degeneration, as it was a cheap and simple remedy, whose efficacy had been firmly established.

Dr. Janet Vaughan said that she taught her hospital out-patients to give themselves intramuscular injections of liver extracts. Even those who at the beginning seemed most unwilling were able to do this, after being shown how several times. Two cubic centimetres of campolon or hepastab was injected into either arm or thigh. This was a very satisfactory method of dealing with these so-called resistant cases of both subacute combined degeneration and pernicious anæmia.

Dr. Kinnier Wilson (Chairman) said that during the discussion rather conflicting statements had been made, so much so that he agreed with Dr. Ferguson in wondering whether all the speakers were referring to the same disease. What was the definition of subacute combined degeneration? Like Dr. Harris and Dr. Langmead, he did not consider it necessary that the type of anæmia should be of the pernicious variety for a diagnosis. He had seen cases whose clinical picture was characteristic,

but in which the anæmia was not of the pernicious kind. Dr. Witts had said that the best prophylaxis for subacute combined degeneration was to treat the pernicious anæmia; this assumed that without treatment the nervous ailment would develop. With that view he (the President) could not agree; cases of pernicious anæmia, in days gone by, at least, ran their course often enough without any development of combined sclerosis in the cord. Moreover, as Dr. Harris had pointed out, cases of the nervous affection were sometimes seen before any special change in the blood picture could be found.

The pathological lesions of sensory peripheral nerves found by Dr. Carmichael were important, and this aspect of the question had been well elucidated by him; but he (the Chairman) doubted whether Dr. Carmichael's view that symptoms with regard to which improvement had taken place had been due to peripheral lesions could be substantiated. It was a mistake to suppose that symptoms arose in the place where lesions were situated. Dr. Carmichael relied, among other points, on the occurrence of segmental limb disorder of sensibility as proof of the peripheral site of the lesions. When the sensory loss affected a segment of a limb, say fingers, or hand, or forearm, etc., it was caused by peripheral nerve involvement, yet Brissaud had shown many years ago that the same kind of segmental loss occurred in cord diseases, such as syringomyelia, and might be due to partial changes over several spinal segments.

Dr. Carmichael had not taken any cases before the age of 40 as possibly doubtful ones, but a subsequent speaker had described a typical example in a person aged 28. The syndrome of subacute combined degeneration was wide, and it was undesirable to restrict it in any way. Characteristic early cases need not show so-called "organic" signs of pyramidal disease.

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